

PATENT APPLICATION

**Methods of Diagnosis of Colorectal Cancer, Compositions and Methods of
Screening for Colorectal Cancer Modulators**

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CROSS-REFERENCES TO RELATED APPLICATIONS

[01] This application is a continuation in part of US Patent Application USSN 09/663,733 filed September 15, 2000, which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[02] The invention relates to the identification of expression profiles and the nucleic acids involved in colorectal cancer, and to the use of such expression profiles and nucleic acids in diagnosis and prognosis of colorectal cancer. The invention further relates to methods for identifying and using candidate agents and/or targets which modulate colorectal cancer.

BACKGROUND OF THE INVENTION

[03] Cancer of the colon and/or rectum (referred to as "colorectal cancer") are significant in Western populations and particularly in the United States. Cancers of the colon and rectum occur in both men and women most commonly after the age of 50. These develop as the result of a pathologic transformation of normal colon epithelium to an invasive cancer. There have been a number of recently characterized genetic alterations that have been implicated in colorectal cancer, including mutations in two classes of genes, tumor-suppressor genes and proto-oncogenes, with recent work suggesting that mutations in DNA repair genes may also be involved in tumorigenesis. For example, inactivating mutations of both alleles of the adenomatous polyposis coli (APC) gene, a tumor suppressor gene, appears to be one of the earliest events in colorectal cancer, and may even be the initiating event. Other genes implicated in colorectal cancer include the MCC gene, the p53 gene, the DCC (deleted in colorectal carcinoma) gene and other chromosome 18q genes, and genes in the TGF- β signaling pathway. For a review, see *Molecular Biology of Colorectal Cancer*, pp. 238-299, in *Curr. Probl. Cancer*, Sept/Oct 1997; see also Willams, *Colorectal Cancer*

(1996); Kinsella & Schofield, *Colorectal Cancer: A Scientific Perspective* (1993); *Colorectal Cancer: Molecular Mechanisms, Premalignant State and its Prevention* (Schmiegel & Scholmerich eds., 2000); *Colorectal Cancer: New Aspects of Molecular Biology and Their Clinical Applications* (Hanski *et al.*, eds 2000); McArdle *et al.*, *Colorectal Cancer* (2000);
 5 Wanebo, *Colorectal Cancer* (1993); Levin, *The American Cancer Society: Colorectal Cancer* (1999); *Treatment of Hepatic Metastases of Colorectal Cancer* (Nordlinger & Jaeck eds., 1993); *Management of Colorectal Cancer* (Dunitz *et al.*, eds. 1998); *Cancer: Principles and Practice of Oncology* (Devita *et al.*, eds. 2001); *Surgical Oncology: Contemporary Principles and Practice* (Kirby *et al.*, eds. 2001); Offit, *Clinical Cancer Genetics: Risk Counseling and*
 10 *Management* (1997); *Radioimmunotherapy of Cancer* (Abrams & Fritzberg eds. 2000); Fleming, *AJCC Cancer Staging Handbook* (1998); *Textbook of Radiation Oncology* (Leibel & Phillips eds. 2000); and *Clinical Oncology* (Abeloff *et al.*, eds. 2000).

[04] Imaging of colorectal cancer for diagnosis has been problematic and limited. In addition, metastasis of the tumor to the lumen, and metastasis of tumor cells to regional lymph nodes are important prognostic factors (*see, e.g., PET in Oncology: Basics and Clinical Application* (Ruhlmann *et al.* eds. 1999). For example, five year survival rates drop from 80 percent in patients with no lymph node metastases to 45 to 50 percent in those patients who do have lymph node metastases. A recent report showed that micrometastases can be detected from lymph nodes using reverse transcriptase-PCR methods based on the presence of mRNA for carcinoembryonic antigen, which has previously been shown to be present in the vast majority of colorectal cancers but not in normal tissues. Liefers *et al.*, *New England J. of Med.* 339(4):223 (1998).

[05] Thus, methods that can be used for diagnosis and prognosis of colorectal cancer would be desirable. Accordingly, provided herein are methods that can be
 25 used in diagnosis and prognosis of colorectal cancer. Further provided are methods that can be used to screen candidate bioactive agents for the ability to modulate colorectal cancer. Additionally, provided herein are molecular targets for therapeutic intervention in colorectal and other cancers.

BRIEF SUMMARY OF THE INVENTION

[06] The present invention provides novel methods for diagnosis and prognosis evaluation for colorectal cancer, as well as methods for screening for compositions which modulate colorectal cancer. Methods of treatment of colorectal cancer, as well as compositions, are also provided herein.

[07] In one aspect, a method of screening drug candidates comprises providing a cell that expresses an expression profile gene selected from those of Table I. The method further includes adding a drug candidate to the cell and determining the effect of the drug candidate on the expression of the expression profile gene.

[08] In one embodiment, the method of screening drug candidates includes comparing the level of expression in the absence of the drug candidate to the level of expression in the presence of the drug candidate, wherein the concentration of the drug candidate can vary when present, and wherein the comparison can occur after addition or removal of the drug candidate. In a preferred embodiment, the cell expresses at least two expression profile genes. The profile genes may show an increase or decrease.

[09] Also provided herein is a method of screening for a bioactive agent capable of binding to a colorectal cancer modulator protein, the method comprising combining the colorectal cancer modulator protein and a candidate bioactive agent, and determining the binding of the candidate agent to the colorectal cancer modulator protein. Preferably the colorectal cancer modulator protein is a product encoded by a gene of Table 1 or Table 2.

[10] Further provided herein is a method for screening for a bioactive agent capable of modulating the activity of a colorectal cancer modulator protein. In one embodiment, the method comprises combining the colorectal cancer modulator protein and a candidate bioactive agent, and determining the effect of the candidate agent on the bioactivity of the colorectal cancer modulator protein. Preferably the colorectal cancer modulator protein is a product encoded by a gene of Table 1 or Table 2.

[11] Also provided is a method of evaluating the effect of a candidate colorectal cancer drug comprising administering the drug to a transgenic animal expressing or over-expressing the colorectal cancer modulator protein, or an animal lacking the colorectal cancer modulator protein, for example as a result of a gene knockout.

[12] Additionally, provided herein is a method of evaluating the effect of a candidate colorectal cancer drug comprising administering the drug to a patient and removing a cell sample from the patient. The expression profile of the cell is then determined. This method may further comprise comparing the expression profile to an expression profile of a healthy individual. In a preferred embodiment, said expression profile includes a gene of Table 1 or Table 2.

[13] Moreover, provided herein is a biochip comprising one or more nucleic acid segments of Table 1 or Table 2, wherein the biochip comprises fewer than 1000 nucleic acid probes. Preferable at least two nucleic acid segments are included.

[14] Furthermore, a method of diagnosing a disorder associated with colorectal cancer is provided. The method comprises determining the expression of a gene of Table 1 or Table 2, in a first tissue type of a first individual, and comparing the distribution to the expression of the gene from a second normal tissue type from the first individual or a second unaffected individual. A difference in the expression indicates that the first individual has a disorder associated with colorectal cancer.

[15] In another aspect, the present invention provides an antibody which specifically binds to a protein encoded by a nucleic acid of Table 1 or Table 2 or a fragment thereof. Preferably the antibody is a monoclonal antibody. The antibody can be a fragment of an antibody such as a single stranded antibody as further described herein, or can be conjugated to another molecule. In one embodiment, the antibody is a humanized antibody.

[16] In one embodiment a method for screening for a bioactive agent capable of interfering with the binding of a colorectal cancer modulating protein (colorectal cancer modulator protein) or a fragment thereof and an antibody which binds to said colorectal cancer modulator protein or fragment thereof. In a preferred embodiment, the method comprises combining a colorectal cancer modulator protein or fragment thereof, a candidate bioactive agent and an antibody which binds to said colorectal cancer modulator protein or fragment thereof. The method further includes determining the binding of said colorectal cancer modulator protein or fragment thereof and said antibody. Wherein there is a change in binding, an agent is identified as an interfering agent. The interfering agent can be an agonist or an antagonist. Preferably, the agent inhibits colorectal cancer.

[17] In a further aspect, a method for inhibiting colorectal cancer is provided. The method can be performed in vitro or in vivo, preferably in vivo to an individual. In a preferred embodiment the method of inhibiting colorectal cancer is provided to an individual with cancer. As described herein, methods of inhibiting colorectal cancer can be performed by administering an inhibitor of the activity of a protein encoded by a nucleic acid of Table 1 or Table 2, including an antisense molecule to the gene or its gene product.

[18] Also provided herein are methods of eliciting an immune response in an individual. In one embodiment a method provided herein comprises administering to an individual a composition comprising a colorectal cancer modulating protein, or a fragment

thereof. In another embodiment, the protein is encoded by a nucleic acid selected from those of Table 1 or Table 2. In another aspect, said composition comprises a nucleic acid comprising a sequence encoding a colorectal cancer modulating protein, or a fragment thereof.

[19] Further provided herein are compositions capable of eliciting an immune response in an individual. In one embodiment, a composition provided herein comprises a colorectal cancer modulating protein, preferably encoded by a nucleic acid of Table 1 or Table 2, or a fragment thereof, and a pharmaceutically acceptable carrier. In another embodiment, said composition comprises a nucleic acid comprising a sequence encoding a colorectal cancer modulating protein, preferably selected from the nucleic acids of Table 1 or Table 2 and a pharmaceutically acceptable carrier.

[20] Also provided are methods of neutralizing the effect of a colorectal cancer protein, or a fragment thereof, comprising contacting an agent specific for said protein with said protein in an amount sufficient to effect neutralization. In another embodiment, the protein is encoded by a nucleic acid selected from those of Table 1 or Table 2.

[21] In another aspect of the invention, a method of treating an individual for colorectal cancer is provided. In one embodiment, the method comprises administering to said individual an inhibitor of a colorectal cancer modulating protein. In another embodiment, the method comprises administering to a patient having colorectal cancer an antibody to a colorectal cancer modulating protein conjugated to a therapeutic moiety. Such a therapeutic moiety can be a cytotoxic agent or a radioisotope.

[22] Compounds and compositions are also provided. Other aspects of the invention will become apparent to the skilled artisan by the following description of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[NOT APPLICABLE]

DETAILED DESCRIPTION OF THE INVENTION

[23] The present invention provides novel methods for diagnosis and prognosis evaluation for colorectal cancer, as well as methods for screening for compositions which modulate colorectal cancer. The methods herein are related to those of U.S. Patent Application Serial No. 09/525,993 and International Patent Application No. PCT/US00/07044, each of which is incorporated herein in its entirety.

[24] By "colorectal cancer" herein is meant a colon and/or rectal tumor or cancer that is classified as Dukes stage A or B as well as metastatic tumors classified as Dukes stage Cor D (see, e.g., Cohen *et al.*, *Cancer of the Colon*, in *Cancer: Principles and Practice of Oncology*, pp. 1144-1197 (Devita *et al.*, eds., 5th ed. 1997); see also Harrison's

5 *Principles of Internal Medicine*, pp. 1289-129 (Wilson *et al.*, eds., 12th ed., 1991). "Treatment, monitoring, detection or modulation of colorectal cancer" includes treatment, monitoring, detection, or modulation of colorectal disease in those patients who have colorectal disease (Dukes stage A, B, C or D) in which gene expression from a gene in Table 1 or 2, is increased or decreased, indicating that the subject is more likely to progress to

10 metastatic disease than a patient who does not have an increase or decrease in gene expression of a gene in Table 1 or 2. In Dukes stage A, the tumor has penetrated into, but not through, the bowel wall. In Dukes stage B, the tumor has penetrated through the bowel wall but there is not yet any lymph involvement. In Dukes stage C, the cancer involves regional lymph nodes. In Dukes stage D, there is distant metastasis, e.g., liver, lung, etc.

5 [25] Table 1 provides unigene cluster identification numbers for the nucleotide sequence of genes that exhibit increased expression in colorectal cancer samples. Tables 1 also provides an exemplar accession number that provides a nucleotide sequence that is part of the unigene cluster. Table 2 provides the nucleic acid and protein sequence of the CBF9 gene as well as the Unigene and Exemplar accession numbers for CBF9.

20 [26] In one aspect, the expression levels of genes are determined in different patient samples for which either diagnosis or prognosis information is desired, to provide expression profiles. An expression profile of a particular sample is essentially a "fingerprint" of the state of the sample; while two states may have any particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the

25 generation of a gene expression profile that is unique to the state of the cell. That is, normal tissue may be distinguished from colorectal cancer tissue, and within colorectal cancer tissue, different prognosis states (good or poor long term survival prospects, for example) may be determined. By comparing expression profiles of colon tissue in known different states, information regarding which genes are important (including both up- and down-

30 regulation of genes) in each of these states is obtained. The identification of sequences that are differentially expressed in colorectal cancer versus normal colon tissue, as well as differential expression resulting in different prognostic outcomes, allows the use of this information in a number of ways. For example, the evaluation of a particular treatment regime may be evaluated: does a chemotherapeutic drug act to improve the long-term

prognosis in a particular patient. Similarly, diagnosis may be done or confirmed by comparing patient samples with the known expression profiles. Furthermore, these gene expression profiles (or individual genes) allow screening of drug candidates with an eye to mimicking or altering a particular expression profile; for example, screening can be done for drugs that suppress the colorectal cancer expression profile or convert a poor prognosis profile to a better prognosis profile. This may be done by making biochips comprising sets of the important colorectal cancer genes, which can then be used in these screens. These methods can also be done on the protein basis; that is, protein expression levels of the colorectal cancer proteins can be evaluated for diagnostic and prognostic purposes or to screen candidate agents. In addition, the colorectal cancer nucleic acid sequences can be administered for gene therapy purposes, including the administration of antisense nucleic acids, or the colorectal cancer proteins (including antibodies and other modulators thereof) administered as therapeutic drugs.

[27] Thus the present invention provides nucleic acid and protein sequences that are differentially expressed in colorectal cancer, herein termed "colorectal cancer sequences". As outlined below, colorectal cancer sequences include those that are up-regulated (i.e. expressed at a higher level) in colorectal cancer, as well as those that are down-regulated (i.e. expressed at a lower level) in colorectal cancer. In a preferred embodiment, the colorectal cancer sequences are from humans; however, as will be appreciated by those in the art, colorectal cancer sequences from other organisms may be useful in animal models of disease and drug evaluation; thus, other colorectal cancer sequences are provided, from vertebrates, including mammals, including rodents (rats, mice, hamsters, guinea pigs, etc.), primates, farm animals (including sheep, goats, pigs, cows, horses, etc). colorectal cancer sequences from other organisms may be obtained using the techniques outlined below.

[28] Colorectal cancer sequences can include both nucleic acid and amino acid sequences. In a preferred embodiment, the colorectal cancer sequences are recombinant nucleic acids. By the term "recombinant nucleic acid" herein is meant nucleic acid, originally formed in vitro, in general, by the manipulation of nucleic acid by polymerases and endonucleases, in a form not normally found in nature. Thus an isolated nucleic acid, in a linear form, or an expression vector formed in vitro by ligating DNA molecules that are not normally joined, are both considered recombinant for the purposes of this invention. It is understood that once a recombinant nucleic acid is made and reintroduced into a host cell or organism, it will replicate non-recombinantly, i.e. using the in vivo cellular machinery of the

host cell rather than in vitro manipulations; however, such nucleic acids, once produced recombinantly, although subsequently replicated non-recombinantly, are still considered recombinant for the purposes of the invention.

[29] Similarly, a "recombinant protein" is a protein made using recombinant techniques, i.e. through the expression of a recombinant nucleic acid as depicted above. A recombinant protein is distinguished from naturally occurring protein by at least one or more characteristics. For example, the protein may be isolated or purified away from some or all of the proteins and compounds with which it is normally associated in its wild type host, and thus may be substantially pure. For example, an isolated protein is unaccompanied by at least some of the material with which it is normally associated in its natural state, preferably constituting at least about 0.5%, more preferably at least about 5% by weight of the total protein in a given sample. A substantially pure protein comprises at least about 75% by weight of the total protein, with at least about 80% being preferred, and at least about 90% being particularly preferred. The definition includes the production of a colorectal cancer protein from one organism in a different organism or host cell. Alternatively, the protein may be made at a significantly higher concentration than is normally seen, through the use of an inducible promoter or high expression promoter, such that the protein is made at increased concentration levels. Alternatively, the protein may be in a form not normally found in nature, as in the addition of an epitope tag or amino acid substitutions, insertions and deletions, as discussed below.

[30] In a preferred embodiment, the colorectal cancer sequences are nucleic acids. As will be appreciated by those in the art and is more fully outlined below, colorectal cancer sequences are useful in a variety of applications, including diagnostic applications, which will detect naturally occurring nucleic acids, as well as screening applications; for example, biochips comprising nucleic acid probes to the colorectal cancer sequences can be generated. In the broadest sense, then, by "nucleic acid" or "oligonucleotide" or grammatical equivalents herein means at least two nucleotides covalently linked together. A nucleic acid of the present invention will generally contain phosphodiester bonds, although in some cases, as outlined below, nucleic acid analogs are included that may have alternate backbones, comprising, for example, phosphoramidate (Beaucage et al., Tetrahedron 49(10):1925 (1993) and references therein; Letsinger, J. Org. Chem. 35:3800 (1970); Sprinzl et al., Eur. J. Biochem. 81:579 (1977); Letsinger et al., Nucl. Acids Res. 14:3487 (1986); Sawai et al, Chem. Lett. 805 (1984), Letsinger et al., J. Am. Chem. Soc. 110:4470 (1988); and Pauwels et al., Chemica Scripta 26:141 91986)),

phosphorothioate (Mag et al., Nucleic Acids Res. 19:1437 (1991); and U.S. Patent No. 5,644,048), phosphordithioate (Briu et al., J. Am. Chem. Soc. 111:2321 (1989), O-methylphosphoramidite linkages (see Eckstein, Oligonucleotides and Analogues: A Practical Approach, Oxford University Press), and peptide nucleic acid backbones and linkages (see Egholm, J. Am. Chem. Soc. 114:1895 (1992); Meier et al., Chem. Int. Ed. Engl. 31:1008 (1992); Nielsen, Nature, 365:566 (1993); Carlsson et al., Nature 380:207 (1996), all of which are incorporated by reference). Other analog nucleic acids include those with positive backbones (Denpcy et al., Proc. Natl. Acad. Sci. USA 92:6097 (1995); non-ionic backbones (U.S. Patent Nos. 5,386,023, 5,637,684, 5,602,240, 5,216,141 and 4,469,863; Kiedrowshi et al., Angew. Chem. Intl. Ed. English 30:423 (1991); Letsinger et al., J. Am. Chem. Soc. 110:4470 (1988); Letsinger et al., Nucleoside & Nucleotide 13:1597 (1994); Chapters 2 and 3, ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y.S. Sanghui and P. Dan Cook; Mesmaeker et al., Bioorganic & Medicinal Chem. Lett. 4:395 (1994); Jeffs et al., J. Biomolecular NMR 34:17 (1994); Tetrahedron Lett. 37:743 (1996)) and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y.S. Sanghui and P. Dan Cook. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids (see Jenkins et al., Chem. Soc. Rev. (1995) pp169-176). Several nucleic acid analogs are described in Rawls, C & E News June 2, 1997 page 35. All of these references are hereby expressly incorporated by reference. These modifications of the ribose-phosphate backbone may be done for a variety of reasons, for example to increase the stability and half-life of such molecules in physiological environments or as probes on a biochip.

[31] As will be appreciated by those in the art, all of these nucleic acid analogs may find use in the present invention. In addition, mixtures of naturally occurring nucleic acids and analogs can be made; alternatively, mixtures of different nucleic acid analogs, and mixtures of naturally occurring nucleic acids and analogs may be made.

[32] Particularly preferred are peptide nucleic acids (PNA) which includes peptide nucleic acid analogs. These backbones are substantially non-ionic under neutral conditions, in contrast to the highly charged phosphodiester backbone of naturally occurring nucleic acids. This results in two advantages. First, the PNA backbone exhibits improved hybridization kinetics. PNAs have larger changes in the melting temperature (T_m) for mismatched versus perfectly matched basepairs. DNA and RNA typically exhibit a 2-4°C drop in T_m for an internal mismatch. With the non-ionic PNA backbone, the drop is closer to

7-9°C. Similarly, due to their non-ionic nature, hybridization of the bases attached to these backbones is relatively insensitive to salt concentration. In addition, PNAs are not degraded by cellular enzymes, and thus can be more stable.

[33] The nucleic acids may be single stranded or double stranded, as specified, or contain portions of both double stranded or single stranded sequence. As will be appreciated by those in the art, the depiction of a single strand ("Watson") also defines the sequence of the other strand ("Crick"); thus the sequences described herein also includes the complement of the sequence. The nucleic acid may be DNA, both genomic and cDNA, RNA or a hybrid, where the nucleic acid contains any combination of deoxyribo- and ribo-nucleotides, and any combination of bases, including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine, isoguanine, etc. As used herein, the term "nucleoside" includes nucleotides and nucleoside and nucleotide analogs, and modified nucleosides such as amino modified nucleosides. In addition, "nucleoside" includes non-naturally occurring analog structures. Thus for example the individual units of a peptide nucleic acid, each containing a base, are referred to herein as a nucleoside.

[34] A colorectal cancer sequence can be initially identified by substantial nucleic acid and/or amino acid sequence homology to the colorectal cancer sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions.

[35] The isolation of mRNA comprises isolating total cellular RNA by disrupting a cell and performing differential centrifugation. Once the total RNA is isolated, mRNA is isolated by making use of the adenine nucleotide residues known to those skilled in the art as a poly (A) tail found on virtually every eukaryotic mRNA molecule at the 3'end thereof. Oligonucleotides composed of only deoxythymidine [oligo(dT)] are linked to cellulose and the oligo(dT)-cellulose packed into small columns. When a preparation of total cellular RNA is passed through such a column, the mRNA molecules bind to the oligo(dT) by the poly (A) tails while the rest of the RNA flows through the column. The bound mRNAs are then eluted from the column and collected.

[36] The colorectal cancer sequences of the invention can be identified as follows. Samples of normal and tumor tissue are applied to biochips comprising nucleic acid probes. The samples are first microdissected, if applicable, and treated as described above for the preparation of mRNA. Suitable biochips are commercially available, for example

from Affymetrix. Gene expression profiles as described herein are generated, and the data analyzed.

[37] In a preferred embodiment, the genes showing changes in expression as between normal and disease states are compared to genes expressed in other normal tissues, including, but not limited to lung, heart, brain, liver, breast, kidney, muscle, prostate, small intestine, large intestine, spleen, bone, and placenta. In a preferred embodiment, those genes identified during the colorectal cancer screen that are expressed in any significant amount in other tissues are removed from the profile, although in some embodiments, this is not necessary. That is, when screening for drugs, it is preferable that the target be disease specific, to minimize possible side effects.

[38] In a preferred embodiment, colorectal cancer sequences are those that are up-regulated in colorectal cancer ; that is, the expression of these genes is higher in colorectal carcinoma as compared to normal colon tissue. "Up-regulation" as used herein means at least about a 1.1 fold change, preferably a 1.5 or two fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred. All accession numbers herein are for the GenBank sequence database and the sequences of the accession numbers are hereby expressly incorporated by reference. GenBank is known in the art, see, e.g., Benson, DA, et al., Nucleic Acids Research 26:1-7 (1998) and <http://www.ncbi.nlm.nih.gov/>. In addition, these genes were found to be expressed in a limited amount or not at all in heart, brain, lung, liver, breast, kidney, prostate, small intestine and spleen.

[39] In a preferred embodiment, colorectal cancer sequences are those that are down-regulated in colorectal cancer ; that is, the expression of these genes is lower in colorectal carcinoma as compared to normal colon tissue. "Down-regulation" as used herein means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred.

[40] Colorectal cancer proteins of the present invention may be classified as secreted proteins, transmembrane proteins or intracellular proteins. In a preferred embodiment the colorectal cancer protein is an intracellular protein. Intracellular proteins may be found in the cytoplasm and/or in the nucleus. Intracellular proteins are involved in all aspects of cellular function and replication (including, for example, signaling pathways); aberrant expression of such proteins results in unregulated or dysregulated cellular processes. For example, many intracellular proteins have enzymatic activity such as protein kinase activity, protein phosphatase activity, protease activity, nucleotide cyclase activity,

polymerase activity and the like. Intracellular proteins also serve as docking proteins that are involved in organizing complexes of proteins, or targeting proteins to various subcellular localizations, and are involved in maintaining the structural integrity of organelles.

[41] An increasingly appreciated concept in characterizing intracellular proteins is the presence in the proteins of one or more motifs for which defined functions have been attributed. In addition to the highly conserved sequences found in the enzymatic domain of proteins, highly conserved sequences have been identified in proteins that are involved in protein-protein interaction. For example, Src-homology-2 (SH2) domains bind tyrosine-phosphorylated targets in a sequence dependent manner. PTB domains, which are distinct from SH2 domains, also bind tyrosine phosphorylated targets. SH3 domains bind to proline-rich targets. In addition, PH domains, tetratricopeptide repeats and WD domains to name only a few, have been shown to mediate protein-protein interactions. Some of these may also be involved in binding to phospholipids or other second messengers. As will be appreciated by one of ordinary skill in the art, these motifs can be identified on the basis of primary sequence; thus, an analysis of the sequence of proteins may provide insight into both the enzymatic potential of the molecule and/or molecules with which the protein may associate.

[42] In a preferred embodiment, the colorectal cancer sequences are transmembrane proteins. Transmembrane proteins are molecules that span the phospholipid bilayer of a cell. They may have an intracellular domain, an extracellular domain, or both. The intracellular domains of such proteins may have a number of functions including those already described for intracellular proteins. For example, the intracellular domain may have enzymatic activity and/or may serve as a binding site for additional proteins. Frequently the intracellular domain of transmembrane proteins serves both roles. For example certain receptor tyrosine kinases have both protein kinase activity and SH2 domains. In addition, autophosphorylation of tyrosines on the receptor molecule itself, creates binding sites for additional SH2 domain containing proteins.

[43] Transmembrane proteins may contain from one to many transmembrane domains. For example, receptor tyrosine kinases, certain cytokine receptors, receptor guanylyl cyclases and receptor serine/threonine protein kinases contain a single transmembrane domain. However, various other proteins including channels and adenylyl cyclases contain numerous transmembrane domains. Many important cell surface receptors are classified as "seven transmembrane domain" proteins, as they contain 7 membrane spanning regions. Important transmembrane protein receptors include, but are not limited to

insulin receptor, insulin-like growth factor receptor, human growth hormone receptor, glucose transporters, transferrin receptor, epidermal growth factor receptor, low density lipoprotein receptor, epidermal growth factor receptor, leptin receptor, interleukin receptors, e.g. IL-1 receptor, IL-2 receptor, etc.

[44] Characteristics of transmembrane domains include approximately 20 consecutive hydrophobic amino acids that may be followed by charged amino acids. Therefore, upon analysis of the amino acid sequence of a particular protein, the localization and number of transmembrane domains within the protein may be predicted.

[45] The extracellular domains of transmembrane proteins are diverse; however, conserved motifs are found repeatedly among various extracellular domains. Conserved structure and/or functions have been ascribed to different extracellular motifs. For example, cytokine receptors are characterized by a cluster of cysteines and a WSXWS (W= tryptophan, S= serine, X=any amino acid) motif. Immunoglobulin-like domains are highly conserved. Mucin-like domains may be involved in cell adhesion and leucine-rich repeats participate in protein-protein interactions.

[46] Many extracellular domains are involved in binding to other molecules. In one aspect, extracellular domains are receptors. Factors that bind the receptor domain include circulating ligands, which may be peptides, proteins, or small molecules such as adenosine and the like. For example, growth factors such as EGF, FGF and PDGF are circulating growth factors that bind to their cognate receptors to initiate a variety of cellular responses. Other factors include cytokines, mitogenic factors, neurotrophic factors and the like. Extracellular domains also bind to cell-associated molecules. In this respect, they mediate cell-cell interactions. Cell-associated ligands can be tethered to the cell for example via a glycosylphosphatidylinositol (GPI) anchor, or may themselves be transmembrane proteins. Extracellular domains also associate with the extracellular matrix and contribute to the maintenance of the cell structure.

[47] Colorectal cancer proteins that are transmembrane are particularly preferred in the present invention as they are good targets for immunotherapeutics, as are described herein. In addition, as outlined below, transmembrane proteins can be also useful in imaging modalities.

[48] It will also be appreciated by those in the art that a transmembrane protein can be made soluble by removing transmembrane sequences, for example through recombinant methods. Furthermore, transmembrane proteins that have been made soluble

can be made to be secreted through recombinant means by adding an appropriate signal sequence.

[49] In a preferred embodiment, the colorectal cancer proteins are secreted proteins; the secretion of which can be either constitutive or regulated. These proteins have a signal peptide or signal sequence that targets the molecule to the secretory pathway. Secreted proteins are involved in numerous physiological events; by virtue of their circulating nature, they serve to transmit signals to various other cell types. The secreted protein may function in an autocrine manner (acting on the cell that secreted the factor), a paracrine manner (acting on cells in close proximity to the cell that secreted the factor) or an endocrine manner (acting on cells at a distance). Thus secreted molecules find use in modulating or altering numerous aspects of physiology. colorectal cancer proteins that are secreted proteins are particularly preferred in the present invention as they serve as good targets for diagnostic markers, for example for blood tests.

[50] A colorectal cancer sequence is initially identified by substantial nucleic acid and/or amino acid sequence homology to the colorectal cancer sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions.

[51] As used herein, the terms "colorectal cancer nucleic acid", "colorectal cancer protein" or "colorectal cancer polynucleotide" or "colorectal cancer-associated transcript" refers to nucleic acid and polypeptide polymorphic variants, alleles, mutants, and interspecies homologs that: (1) have a nucleotide sequence that has greater than about 60% nucleotide sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater nucleotide sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more nucleotides, to a nucleotide sequence of or associated with a unigene cluster of Tables 1 or Table 2; (2) bind to antibodies, e.g., polyclonal antibodies, raised against an immunogen comprising an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Table 1 or Table 2, and conservatively modified variants thereof; (3) specifically hybridize under stringent hybridization conditions to a nucleic acid sequence, or the complement thereof of Table 1 or Table 2 and conservatively modified variants thereof or (4) have an amino acid sequence that has greater than about 60% amino acid sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater amino sequence identity, preferably over a region of over a region of at least about

25, 50, 100, 200, 500, 1000, or more amino acid, to an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Table 1 or Table 2. A polynucleotide or polypeptide sequence is typically from a mammal including, but not limited to, primate, e.g., human; rodent, e.g., rat, mouse, hamster; cow, pig, horse, sheep, or other mammal. A "colorectal cancer polypeptide" and a "colorectal cancer polynucleotide," include both naturally occurring or recombinant.

[52] Homology in this context means sequence similarity or identity, with identity being preferred. A preferred comparison for homology purposes is to compare the sequence containing sequencing errors to the correct sequence. This homology will be determined using standard techniques known in the art, including, but not limited to, the local homology algorithm of Smith & Waterman, Adv. Appl. Math. 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, J. Mol. Biol. 48:443 (1970), by the search for similarity method of Pearson & Lipman, PNAS USA 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Drive, Madison, WI), the Best Fit sequence program described by Devereux et al., Nucl. Acid Res. 12:387-395 (1984), preferably using the default settings, or by inspection.

[53] In a preferred embodiment, the sequences which are used to determine sequence identity or similarity are selected from the sequences set forth in Table 1 or Table 2. In one embodiment the sequences utilized herein are those set forth in Table 1 or Table 2. In another embodiment, the sequences are naturally occurring allelic variants of the sequences set forth in Table 1 or Table 2. In another embodiment, the sequences are sequence variants as further described herein.

[54] The terms "identical" or percent "identity," in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (i.e., about 60% identity, preferably 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity over a specified region, when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection (see, e.g., NCBI web site <http://www.ncbi.nlm.nih.gov/BLAST/> or the like). Such sequences are then said to be "substantially identical." This definition also refers to, or may be applied to, the complement of a test sequence. The definition also includes sequences that have deletions

and/or additions, as well as those that have substitutions, as well as naturally occurring, e.g., polymorphic or allelic variants, and man-made variants. As described below, the preferred algorithms can account for gaps and the like. Preferably, identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length.

[55] For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated.

Preferably, default program parameters can be used, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

[56] A "comparison window", as used herein, includes reference to a segment of one of the number of contiguous positions selected from the group consisting typically of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Nat'l. Acad. Sci. USA* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (*see, e.g., Current Protocols in Molecular Biology* (Ausubel *et al.*, eds. 1995 supplement)).

[57] Preferred examples of algorithms that are suitable for determining percent sequence identity and sequence similarity include the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.*, *Nuc. Acids Res.* 25:3389-3402 (1997) and Altschul *et al.*, *J. Mol. Biol.* 215:403-410 (1990). BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>).

This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*).

5 These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, e.g., for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

[58] The BLAST algorithm also performs a statistical analysis of the similarity between two sequences (see, e.g., Karlin & Altschul, *Proc. Nat'l. Acad. Sci. USA* 90:5873-5878 (1993)). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference nucleic acid is less than about 0.2, more preferably less than about 0.01, and most preferably less than about 0.001. Log values may be large negative numbers, e.g., 5, 10, 20, 30, 40, 40, 70, 90, 110, 150, 170, etc.

[59] In one embodiment, the nucleic acid homology is determined through hybridization studies. Thus, for example, nucleic acids which hybridize under high stringency to the nucleic acid sequences which encode the peptides identified in Table 1 or Table 2, or their complements, are considered a colorectal cancer sequence. High stringency

conditions are known in the art; see for example Maniatis et al., *Molecular Cloning: A Laboratory Manual*, 2d Edition, 1989, and *Short Protocols in Molecular Biology*, ed. Ausubel, et al., both of which are hereby incorporated by reference. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences

5 hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen, *Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Acid Probes*, "Overview of principles of hybridization and the strategy of nucleic acid assays" (1993). Generally, stringent conditions are selected to be about 5-10°C lower than the thermal melting point (T_m) for the specific sequence at a
10 defined ionic strength pH. The T_m is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m , 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M
15 sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (e.g. 10 to 50 nucleotides) and at least about 60°C for long probes (e.g. greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide.

[60] In another embodiment, less stringent hybridization conditions are
20 used; for example, moderate or low stringency conditions may be used, as are known in the art; see Maniatis and Ausubel, *supra*, and Tijssen, *supra*. For selective or specific hybridization, a positive signal is at least two times background, preferably 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42°C, or, 5x SSC, 1% SDS, incubating
25 at 65°C, with wash in 0.2x SSC, and 0.1% SDS at 65°C.

[61] Nucleic acids that do not hybridize to each other under stringent
30 conditions are still substantially identical if the polypeptides which they encode are substantially identical. This occurs, for example, when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary "moderately stringent hybridization conditions" include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 1X SSC at 45°C. A positive hybridization is at least twice background. Those of ordinary skill will readily

recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency. Additional guidelines for determining hybridization parameters are provided in numerous reference, e.g., and *Current Protocols in Molecular Biology*, ed. Ausubel, *et al.*

[62] For PCR, a temperature of about 36°C is typical for low stringency amplification, although annealing temperatures may vary between about 32°C and 48°C depending on primer length. For high stringency PCR amplification, a temperature of about 62°C is typical, although high stringency annealing temperatures can range from about 50°C to about 65°C, depending on the primer length and specificity. Typical cycle conditions for both high and low stringency amplifications include a denaturation phase of 90°C - 95°C for 30 sec - 2 min., an annealing phase lasting 30 sec. - 2 min., and an extension phase of about 72°C for 1 - 2 min. Protocols and guidelines for low and high stringency amplification reactions are provided, e.g., in Innis *et al.*, *PCR Protocols, A Guide to Methods and Applications* (1990).

[63] In addition, the colorectal cancer nucleic acid sequences of the invention are fragments of larger genes, i.e. they are nucleic acid segments. "Genes" in this context includes coding regions, non-coding regions, and mixtures of coding and non-coding regions. Accordingly, as will be appreciated by those in the art, using the sequences provided herein, additional sequences of the colorectal cancer genes can be obtained, using techniques well known in the art for cloning either longer sequences or the full length sequences; see Maniatis *et al.*, and Ausubel, *et al.*, *supra*, hereby expressly incorporated by reference.

[64] An indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid. Thus, a polypeptide is typically substantially identical to a second polypeptide, e.g., where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described above. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequences.

[65] Once the colorectal cancer nucleic acid is identified, it can be cloned and, if necessary, its constituent parts recombined to form the entire colorectal cancer nucleic acid. Once isolated from its natural source, e.g., contained within a plasmid or other vector

or excised therefrom as a linear nucleic acid segment, the recombinant colorectal cancer nucleic acid can be further-used as a probe to identify and isolate other colorectal cancer nucleic acids, for example additional coding regions. It can also be used as a "precursor" nucleic acid to make modified or variant colorectal cancer nucleic acids and proteins.

5 [66] The colorectal cancer nucleic acids of the present invention are used in several ways. In a first embodiment, nucleic acid probes to the colorectal cancer nucleic acids are made and attached to biochips to be used in screening and diagnostic methods, as outlined below, or for administration, for example for gene therapy and/or antisense applications. Alternatively, the colorectal cancer nucleic acids that include coding regions of colorectal cancer proteins can be put into expression vectors for the expression of colorectal cancer proteins, again either for screening purposes or for administration to a patient.

10 [67] In a preferred embodiment, nucleic acid probes to colorectal cancer nucleic acids (both the nucleic acid sequences encoding peptides outlined in the Table 1 or Table 2 and/or the complements thereof) are made. The nucleic acid probes attached to the biochip are designed to be substantially complementary to the colorectal cancer nucleic acids, i.e. the target sequence (either the target sequence of the sample or to other probe sequences, for example in sandwich assays), such that hybridization of the target sequence and the probes of the present invention occurs. As outlined below, this complementarity need not be perfect; there may be any number of base pair mismatches which will interfere with hybridization between the target sequence and the single stranded nucleic acids of the present invention. However, if the number of mutations is so great that no hybridization can occur under even the least stringent of hybridization conditions, the sequence is not a complementary target sequence. Thus, by "substantially complementary" herein is meant that the probes are sufficiently complementary to the target sequences to hybridize under normal reaction conditions, particularly high stringency conditions, as outlined herein.

20 [68] A nucleic acid probe is generally single stranded but can be partially single and partially double stranded. The strandedness of the probe is dictated by the structure, composition, and properties of the target sequence. In general, the nucleic acid probes range from about 8 to about 100 bases long, with from about 10 to about 80 bases being preferred, and from about 30 to about 50 bases being particularly preferred. That is, generally whole genes are not used. In some embodiments, much longer nucleic acids can be used, up to hundreds of bases.

30 [69] In a preferred embodiment, more than one probe per sequence is used, with either overlapping probes or probes to different sections of the target being used. That

is, two, three, four or more probes, with three being preferred, are used to build in a redundancy for a particular target. The probes can be overlapping (i.e. have some sequence in common), or separate.

[70] As will be appreciated by those in the art, nucleic acids can be attached or immobilized to a solid support in a wide variety of ways. By "immobilized" and grammatical equivalents herein is meant the association or binding between the nucleic acid probe and the solid support is sufficient to be stable under the conditions of binding, washing, analysis, and removal as outlined below. The binding can be covalent or non-covalent. By "non-covalent binding" and grammatical equivalents herein is meant one or more of either electrostatic, hydrophilic, and hydrophobic interactions. Included in non-covalent binding is the covalent attachment of a molecule, such as, streptavidin to the support and the non-covalent binding of the biotinylated probe to the streptavidin. By "covalent binding" and grammatical equivalents herein is meant that the two moieties, the solid support and the probe, are attached by at least one bond, including sigma bonds, pi bonds and coordination bonds. Covalent bonds can be formed directly between the probe and the solid support or can be formed by a cross linker or by inclusion of a specific reactive group on either the solid support or the probe or both molecules. Immobilization may also involve a combination of covalent and non-covalent interactions.

[71] In general, the probes are attached to the biochip in a wide variety of ways, as will be appreciated by those in the art. As described herein, the nucleic acids can either be synthesized first, with subsequent attachment to the biochip, or can be directly synthesized on the biochip.

[72] The biochip comprises a suitable solid substrate. By "substrate" or "solid support" or other grammatical equivalents herein is meant any material that can be modified to contain discrete individual sites appropriate for the attachment or association of the nucleic acid probes and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates are very large, and include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, Teflon, etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, etc. In general, the substrates allow optical detection and do not appreciably fluoresce. A preferred substrate is described in copending application entitled

Reusable Low Fluorescent Plastic Biochip, U.S. Application Serial No. 09/270,214, filed March 15, 1999, herein incorporated by reference in its entirety.

[73] Generally the substrate is planar, although as will be appreciated by those in the art, other configurations of substrates may be used as well. For example, the probes may be placed on the inside surface of a tube, for flow-through sample analysis to minimize sample volume. Similarly, the substrate may be flexible, such as a flexible foam, including closed cell foams made of particular plastics.

[74] In a preferred embodiment, the surface of the biochip and the probe may be derivatized with chemical functional groups for subsequent attachment of the two.

Thus, for example, the biochip is derivatized with a chemical functional group including, but not limited to, amino groups, carboxy groups, oxo groups and thiol groups, with amino groups being particularly preferred. Using these functional groups, the probes can be attached using functional groups on the probes. For example, nucleic acids containing amino groups can be attached to surfaces comprising amino groups, for example using linkers as are known in the art; for example, homo- or hetero-bifunctional linkers as are well known (see 1994 Pierce Chemical Company catalog, technical section on cross-linkers, pages 155-200, incorporated herein by reference). In addition, in some cases, additional linkers, such as alkyl groups (including substituted and heteroalkyl groups) may be used.

[75] In this embodiment, the oligonucleotides are synthesized as is known in the art, and then attached to the surface of the solid support. As will be appreciated by those skilled in the art, either the 5' or 3' terminus may be attached to the solid support, or attachment may be via an internal nucleoside.

[76] In an additional embodiment, the immobilization to the solid support may be very strong, yet non-covalent. For example, biotinylated oligonucleotides can be made, which bind to surfaces covalently coated with streptavidin, resulting in attachment.

[01] Alternatively, the oligonucleotides may be synthesized on the surface, as is known in the art. For example, photoactivation techniques utilizing photopolymerization compounds and techniques are used. In a preferred embodiment, the nucleic acids can be synthesized in situ, using well known photolithographic techniques, such as those described in WO 95/25116; WO 95/35505; U.S. Patent Nos. 5,700,637 and 5,445,934; and references cited within, all of which are expressly incorporated by reference; these methods of attachment form the basis of the Affimetrix GeneChip™ technology.

[78] In a preferred embodiment, colorectal cancer nucleic acids encoding colorectal cancer proteins are used to make a variety of expression vectors to express colorectal cancer proteins which can then be used in screening assays, as described below. The expression vectors may be either self-replicating extrachromosomal vectors or vectors which integrate into a host genome. Generally, these expression vectors include transcriptional and translational regulatory nucleic acid operably linked to the nucleic acid encoding the colorectal cancer protein. The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

[79] Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice. The transcriptional and translational regulatory nucleic acid will generally be appropriate to the host cell used to express the colorectal cancer protein; for example, transcriptional and translational regulatory nucleic acid sequences from *Bacillus* are preferably used to express the colorectal cancer protein in *Bacillus*. Numerous types of appropriate expression vectors, and suitable regulatory sequences are known in the art for a variety of host cells.

[80] In general, the transcriptional and translational regulatory sequences may include, but are not limited to, promoter sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and stop sequences, and enhancer or activator sequences. In a preferred embodiment, the regulatory sequences include a promoter and transcriptional start and stop sequences.

[81] Promoter sequences encode either constitutive or inducible promoters. The promoters may be either naturally occurring promoters or hybrid promoters. Hybrid

promoters, which combine elements of more than one promoter, are also known in the art, and are useful in the present invention.

[82] In addition, the expression vector may comprise additional elements. For example, the expression vector may have two replication systems, thus allowing it to be maintained in two organisms, for example in mammalian or insect cells for expression and a procaryotic host for cloning and amplification. Furthermore, for integrating expression vectors, the expression vector contains at least one sequence homologous to the host cell genome, and preferably two homologous sequences which flank the expression construct. The integrating vector may be directed to a specific locus in the host cell by selecting the appropriate homologous sequence for inclusion in the vector. Constructs for integrating vectors are well known in the art.

[83] In addition, in a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

[84] The colorectal cancer proteins of the present invention are produced by culturing a host cell transformed with an expression vector containing nucleic acid encoding a colorectal cancer protein, under the appropriate conditions to induce or cause expression of the colorectal cancer protein. The conditions appropriate for colorectal cancer protein expression will vary with the choice of the expression vector and the host cell, and will be easily ascertained by one skilled in the art through routine experimentation. For example, the use of constitutive promoters in the expression vector will require optimizing the growth and proliferation of the host cell, while the use of an inducible promoter requires the appropriate growth conditions for induction. In addition, in some embodiments, the timing of the harvest is important. For example, the baculoviral systems used in insect cell expression are lytic viruses, and thus harvest time selection can be crucial for product yield.

[85] Appropriate host cells include yeast, bacteria, archaeobacteria, fungi, and insect and animal cells, including mammalian cells. Of particular interest are *Drosophila* melanogaster cells, *Saccharomyces cerevisiae* and other yeasts, *E. coli*, *Bacillus subtilis*, Sf9 cells, C129 cells, 293 cells, *Neurospora*, BHK, CHO, COS, HeLa cells, THP1 cell line (a macrophage cell line) and human cells and cell lines.

[86] In a preferred embodiment, the colorectal cancer proteins are expressed in mammalian cells. Mammalian expression systems are also known in the art, and include retroviral systems. A preferred expression vector system is a retroviral vector system such as is generally described in PCT/US97/01019 and PCT/US97/01048, both of which are

hereby expressly incorporated by reference. Of particular use as mammalian promoters are the promoters from mammalian viral genes, since the viral genes are often highly expressed and have a broad host range. Examples include the SV40 early promoter, mouse mammary tumor virus LTR promoter, adenovirus major late promoter, herpes simplex virus promoter, and the CMV promoter. Typically, transcription termination and polyadenylation sequences recognized by mammalian cells are regulatory regions located 3' to the translation stop codon and thus, together with the promoter elements, flank the coding sequence. Examples of transcription terminator and polyadenylation signals include those derived from SV40.

[87] The methods of introducing exogenous nucleic acid into mammalian hosts, as well as other hosts, is well known in the art, and will vary with the host cell used. Techniques include dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, viral infection, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei.

[88] In a preferred embodiment, colorectal cancer proteins are expressed in bacterial systems. Bacterial expression systems are well known in the art. Promoters from bacteriophage may also be used and are known in the art. In addition, synthetic promoters and hybrid promoters are also useful; for example, the tac promoter is a hybrid of the trp and lac promoter sequences. Furthermore, a bacterial promoter can include naturally occurring promoters of non-bacterial origin that have the ability to bind bacterial RNA polymerase and initiate transcription. In addition to a functioning promoter sequence, an efficient ribosome binding site is desirable. The expression vector may also include a signal peptide sequence that provides for secretion of the colorectal cancer protein in bacteria. The protein is either secreted into the growth media (gram-positive bacteria) or into the periplasmic space, located between the inner and outer membrane of the cell (gram-negative bacteria). The bacterial expression vector may also include a selectable marker gene to allow for the selection of bacterial strains that have been transformed. Suitable selection genes include genes which render the bacteria resistant to drugs such as ampicillin, chloramphenicol, erythromycin, kanamycin, neomycin and tetracycline. Selectable markers also include biosynthetic genes, such as those in the histidine, tryptophan and leucine biosynthetic pathways. These components are assembled into expression vectors. Expression vectors for bacteria are well known in the art, and include vectors for *Bacillus subtilis*, *E. coli*, *Streptococcus cremoris*, and *Streptococcus lividans*, among others. The bacterial expression vectors are transformed

into bacterial host cells using techniques well known in the art, such as calcium chloride treatment, electroporation, and others.

[89] In one embodiment, colorectal cancer proteins are produced in insect cells. Expression vectors for the transformation of insect cells, and in particular, baculovirus-based expression vectors, are well known in the art.

[90] In a preferred embodiment, colorectal cancer protein is produced in yeast cells. Yeast expression systems are well known in the art, and include expression vectors for *Saccharomyces cerevisiae*, *Candida albicans* and *C. maltosa*, *Hansenula polymorpha*, *Kluyveromyces fragilis* and *K. lactis*, *Pichia guilliermondii* and *P. pastoris*, *Schizosaccharomyces pombe*, and *Yarrowia lipolytica*.

[91] The colorectal cancer protein may also be made as a fusion protein, using techniques well known in the art. Thus, for example, for the creation of monoclonal antibodies, if the desired epitope is small, the colorectal cancer protein may be fused to a carrier protein to form an immunogen. Alternatively, the colorectal cancer protein may be made as a fusion protein to increase expression, or for other reasons. For example, when the colorectal cancer protein is a colorectal cancer peptide, the nucleic acid encoding the peptide may be linked to other nucleic acid for expression purposes.

[92] In one embodiment, the colorectal cancer nucleic acids, proteins and antibodies of the invention are labeled. By "labeled" herein is meant that a compound has at least one element, isotope or chemical compound attached to enable the detection of the compound. In general, labels fall into three classes: a) isotopic labels, which may be radioactive or heavy isotopes; b) immune labels, which may be antibodies or antigens; and c) colored or fluorescent dyes. The labels may be incorporated into the colorectal cancer nucleic acids, proteins and antibodies at any position. For example, the label should be capable of producing, either directly or indirectly, a detectable signal. The detectable moiety may be a radioisotope, such as ^3H , ^{14}C , ^{32}P , ^{35}S , or ^{125}I , a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase. Any method known in the art for conjugating the antibody to the label may be employed, including those methods described by Hunter et al., *Nature*, 144:945 (1962); David et al., *Biochemistry*, 13:1014 (1974); Pain et al., *J. Immunol. Meth.*, 40:219 (1981); and Nygren, *J. Histochem. and Cytochem.*, 30:407 (1982).

[93] Accordingly, the present invention also provides colorectal cancer protein sequences. A colorectal cancer protein of the present invention may be identified in

several ways. "Protein" in this sense includes proteins, polypeptides, and peptides terms which are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers, those containing modified residues, and non-naturally occurring amino acid polymer.

[94] As will be appreciated by those in the art, the nucleic acid sequences of the invention can be used to generate protein sequences. There are a variety of ways to do this, including cloning the entire gene and verifying its frame and amino acid sequence, or by comparing it to known sequences to search for homology to provide a frame, assuming the colorectal cancer protein has homology to some protein in the database being used. Generally, the nucleic acid sequences are input into a program that will search all three frames for homology. This is done in a preferred embodiment using the following NCBI Advanced BLAST parameters. The program is blastx or blastn. The database is nr. The input data is as "Sequence in FASTA format". The organism list is "none". The "expect" is 10; the filter is default. The "descriptions" is 500, the "alignments" is 500, and the "alignment view" is pairwise. The "Query Genetic Codes" is standard (1). The matrix is BLOSUM62; gap existence cost is 11, per residue gap cost is 1; and the lambda ratio is .85 default. This results in the generation of a putative protein sequence.

[95] Also included within one embodiment of colorectal cancer proteins are amino acid variants of the naturally occurring sequences, as determined herein. Preferably, the variants are preferably greater than about 75% homologous to the wild-type sequence, more preferably greater than about 80%, even more preferably greater than about 85% and most preferably greater than 90%. In some embodiments the homology will be as high as about 93 to 95 or 98%. As for nucleic acids, homology in this context means sequence similarity or identity, with identity being preferred. This homology will be determined using standard techniques known in the art as are outlined above for the nucleic acid homologies.

[96] Colorectal cancer proteins of the present invention may be shorter or longer than the wild type amino acid sequences. Thus, in a preferred embodiment, included within the definition of colorectal cancer proteins are portions or fragments of the wild type sequences. herein. In addition, as outlined above, the colorectal cancer nucleic acids of the invention may be used to obtain additional coding regions, and thus additional protein sequence, using techniques known in the art.

[97] In a preferred embodiment, the colorectal cancer proteins are derivative or variant colorectal cancer proteins as compared to the wild-type sequence. That is, as outlined more fully below, the derivative colorectal cancer peptide will contain at least one amino acid substitution, deletion or insertion, with amino acid substitutions being particularly preferred. The amino acid substitution, insertion or deletion may occur at any residue within the colorectal cancer peptide.

[98] Also included in an embodiment of colorectal cancer proteins of the present invention are amino acid sequence variants. These variants fall into one or more of three classes: substitutional, insertional or deletional variants. These variants ordinarily are prepared by site specific mutagenesis of nucleotides in the DNA encoding the colorectal cancer protein, using cassette or PCR mutagenesis or other techniques well known in the art, to produce DNA encoding the variant, and thereafter expressing the DNA in recombinant cell culture as outlined above. However, variant colorectal cancer protein fragments having up to about 100-150 residues may be prepared by in vitro synthesis using established techniques. Amino acid sequence variants are characterized by the predetermined nature of the variation, a feature that sets them apart from naturally occurring allelic or interspecies variation of the colorectal cancer protein amino acid sequence. The variants typically exhibit the same qualitative biological activity as the naturally occurring analogue, although variants can also be selected which have modified characteristics as will be more fully outlined below.

[99] While the site or region for introducing an amino acid sequence variation is predetermined, the mutation per se need not be predetermined. For example, in order to optimize the performance of a mutation at a given site, random mutagenesis may be conducted at the target codon or region and the expressed colorectal cancer variants screened for the optimal combination of desired activity. Techniques for making substitution mutations at predetermined sites in DNA having a known sequence are well known, for example, M13 primer mutagenesis and PCR mutagenesis. Screening of the mutants is done using assays of colorectal cancer protein activities.

[100] Amino acid substitutions are typically of single residues; insertions usually will be on the order of from about 1 to 20 amino acids, although considerably larger insertions may be tolerated. Deletions range from about 1 to about 20 residues, although in some cases deletions may be much larger.

[101] Substitutions, deletions, insertions or any combination thereof may be used to arrive at a final derivative. Generally these changes are done on a few amino acids to minimize the alteration of the molecule. However, larger changes may be tolerated in certain

circumstances. When small alterations in the characteristics of the colorectal cancer protein are desired, substitutions are generally made in accordance with the following chart:

Chart I

Original Residue	Exemplary Substitutions
Ala	Ser
Arg	Lys
Asn	Gln, His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Pro
His	Asn, Gln
Ile	Leu, Val
Leu	Ile, Val
Lys	Arg, Gln, Glu
Met	Leu, Ile
Phe	Met, Leu, Tyr
Ser	Thr
Thr	Ser
Trp	Tyr
Tyr	Trp, Phe
Val	Ile, Leu

[102] Substantial changes in function or immunological identity are made by selecting substitutions that are less conservative than those shown in Chart I. For example, substitutions may be made which more significantly affect: the structure of the polypeptide backbone in the area of the alteration, for example the alpha-helical or beta-sheet structure; the charge or hydrophobicity of the molecule at the target site; or the bulk of the side chain. The substitutions which in general are expected to produce the greatest changes in the polypeptide's properties are those in which (a) a hydrophilic residue, e.g. seryl or threonyl is substituted for (or by) a hydrophobic residue, e.g. leucyl, isoleucyl, phenylalanyl, valyl or alanyl; (b) a cysteine or proline is substituted for (or by) any other residue; (c) a residue

having an electropositive side chain, e.g. lysyl, arginyl, or histidyl, is substituted for (or by) an electronegative residue, e.g. glutamyl or aspartyl; or (d) a residue having a bulky side chain, e.g. phenylalanine, is substituted for (or by) one not having a side chain, e.g. glycine.

[103] The variants typically exhibit the same qualitative biological activity and will elicit the same immune response as the naturally-occurring analogue, although variants also are selected to modify the characteristics of the colorectal cancer proteins as needed. Alternatively, the variant may be designed such that the biological activity of the colorectal cancer protein is altered. For example, glycosylation sites may be altered or removed.

[104] Covalent modifications of colorectal cancer polypeptides are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a colorectal cancer polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C-terminal residues of a colorectal cancer polypeptide. Derivatization with bifunctional agents is useful, for instance, for crosslinking colorectal cancer to a water-insoluble support matrix or surface for use in the method for purifying anti-colorectal cancer antibodies or screening assays, as is more fully described below. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxy-succinimide esters, for example, esters with 4-azido-salicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis-(succinimidyl-propionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)-dithio]propanoate.

[01] Other modifications include deamidation of glutamyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl, threonyl or tyrosyl residues, methylation of the α -amino groups of lysine, arginine, and histidine side chains [T.E. Creighton, *Proteins: Structure and Molecular Properties*, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

[106] Another type of covalent modification of the colorectal cancer polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence colorectal cancer polypeptide, and/or adding one or more glycosylation sites that are not present in the native sequence colorectal cancer polypeptide.

[107] Addition of glycosylation sites to colorectal cancer polypeptides may be accomplished by altering the amino acid sequence thereof. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence colorectal cancer polypeptide (for O-linked glycosylation sites). The colorectal cancer amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the colorectal cancer polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

[108] Another means of increasing the number of carbohydrate moieties on the colorectal cancer polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, colorectal cancer Crit. Rev. Biochem., pp. 259-306 (1981).

[109] Removal of carbohydrate moieties present on the colorectal cancer polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo-and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

[110] Another type of covalent modification of colorectal cancer comprises linking the colorectal cancer polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol, polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

[111] colorectal cancer polypeptides of the present invention may also be modified in a way to form chimeric molecules comprising a colorectal cancer polypeptide fused to another, heterologous polypeptide or amino acid sequence. In one embodiment, such a chimeric molecule comprises a fusion of a colorectal cancer polypeptide with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino-or carboxyl-terminus of the colorectal cancer polypeptide. The presence of such epitope-tagged forms of a colorectal cancer polypeptide can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the colorectal cancer polypeptide to be readily purified by affinity purification

using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. In an alternative embodiment, the chimeric molecule may comprise a fusion of a colorectal cancer polypeptide with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule, such a fusion could be to the Fc region of an IgG molecule.

[112] Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., Science, 255:192-194 (1992)]; tubulin epitope peptide [Skinner et al., J. Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., Proc. Natl. Acad. Sci. USA, 87:6393-6397 (1990)].

[113] Also included with the definition of colorectal cancer protein in one embodiment are other colorectal cancer proteins of the colorectal cancer family, and colorectal cancer proteins from other organisms, which are cloned and expressed as outlined below. Thus, probe or degenerate polymerase chain reaction (PCR) primer sequences may be used to find other related colorectal cancer proteins from humans or other organisms. As will be appreciated by those in the art, particularly useful probe and/or PCR primer sequences include the unique areas of the colorectal cancer nucleic acid sequence. As is generally known in the art, preferred PCR primers are from about 15 to about 35 nucleotides in length, with from about 20 to about 30 being preferred, and may contain inosine as needed. The conditions for the PCR reaction are well known in the art.

[114] In addition, as is outlined herein, colorectal cancer proteins can be made that are longer than those depicted in the Table 1 or Table 2 for example, by the elucidation of additional sequences, the addition of epitope or purification tags, the addition of other fusion sequences, etc.

[115] Colorectal cancer proteins may also be identified as being encoded by colorectal cancer nucleic acids. Thus, colorectal cancer proteins are encoded by nucleic acids that will hybridize to the sequences of the sequence listings, or their complements, as outlined herein.

[116] In a preferred embodiment, when the colorectal cancer protein is to be used to generate antibodies, for example for immunotherapy, the colorectal cancer protein should share at least one epitope or determinant with the full length protein. By "epitope" or "determinant" herein is meant a portion of a protein which will generate and/or bind an antibody or T-cell receptor in the context of MHC. Thus, in most instances, antibodies made to a smaller colorectal cancer protein will be able to bind to the full length protein. In a preferred embodiment, the epitope is unique; that is, antibodies generated to a unique epitope show little or no cross-reactivity. In a preferred embodiment, the epitope is selected from a peptide encoded by a nucleic acid of Table 1. In another preferred embodiment, the epitope is selected from the CBF9 peptide sequence shown in Table 2.

[117] In one embodiment, the term "antibody" includes antibody fragments, as are known in the art, including Fab, Fab2, single chain antibodies (Fv for example), chimeric antibodies, etc., either produced by the modification of whole antibodies or those synthesized de novo using recombinant DNA technologies.

[118] Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the CBF9 peptide of Table 2, or a peptide encoded by a nucleic acid of Table 1 or fragment thereof or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

[119] The antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized in vitro. The immunizing agent will typically include the CBF9 polypeptide or a peptide encoded by a

nucleic acid of Table 1 or a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

[120] In one embodiment, the antibodies are bispecific antibodies.

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for a colorectal cancer protein or a fragment thereof, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit, preferably one that is tumor specific.

[121] In a preferred embodiment, the antibodies to colorectal cancer are capable of reducing or eliminating the biological function of colorectal cancer, as is described below. That is, the addition of anti-colorectal cancer antibodies (either polyclonal or preferably monoclonal) to colorectal cancer (or cells containing colorectal cancer) may reduce or eliminate the colorectal cancer activity. Generally, at least a 25% decrease in activity is preferred, with at least about 50% being particularly preferred and about a 95-100% decrease being especially preferred.

[122] In a preferred embodiment the antibodies to the colorectal cancer proteins are humanized antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric molecules of immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues form a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired

specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-329 (1988); and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)].

[123] Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as import residues, which are typically taken from an import variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such humanized antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

[124] Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, p. 77 (1985) and Boerner et al., J. Immunol., 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire.

This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., *Bio/Technology* 10, 779-783 (1992); Lonberg et al., *Nature* 368 856-859 (1994); Morrison, *Nature* 368, 812-13 (1994); Fishwild et al., *Nature Biotechnology* 14, 845-51 (1996); Neuberger, *Nature Biotechnology* 14, 826 (1996); Lonberg and Huszar, *Intern. Rev. Immunol.* 13 65-93 (1995).

[125] By immunotherapy is meant treatment of colorectal cancer with an antibody raised against colorectal cancer proteins. As used herein, immunotherapy can be passive or active. Passive immunotherapy as defined herein is the passive transfer of antibody to a recipient (patient). Active immunization is the induction of antibody and/or T-cell responses in a recipient (patient). Induction of an immune response is the result of providing the recipient with an antigen to which antibodies are raised. As appreciated by one of ordinary skill in the art, the antigen may be provided by injecting a polypeptide against which antibodies are desired to be raised into a recipient, or contacting the recipient with a nucleic acid capable of expressing the antigen and under conditions for expression of the antigen.

[126] In a preferred embodiment the colorectal cancer proteins against which antibodies are raised are secreted proteins as described above. Without being bound by theory, antibodies used for treatment, bind and prevent the secreted protein from binding to its receptor, thereby inactivating the secreted colorectal cancer protein.

[01] In another preferred embodiment, the colorectal cancer protein to which antibodies are raised is a transmembrane protein. Without being bound by theory, antibodies used for treatment, bind the extracellular domain of the colorectal cancer protein and prevent it from binding to other proteins, such as circulating ligands or cell-associated molecules. The antibody may cause down-regulation of the transmembrane colorectal cancer protein. As will be appreciated by one of ordinary skill in the art, the antibody may be a competitive, non-competitive or uncompetitive inhibitor of protein binding to the extracellular domain of the colorectal cancer protein. The antibody is also an antagonist of the colorectal cancer protein. Further, the antibody prevents activation of the transmembrane colorectal cancer protein. In one aspect, when the antibody prevents the binding of other molecules to the colorectal cancer protein, the antibody prevents growth of the cell. The antibody also sensitizes the cell to cytotoxic agents, including, but not limited to TNF- α , TNF- β , IL-1, INF- γ and IL-2, or chemotherapeutic agents including 5FU, vinblastine,

actinomycin D, cisplatin, methotrexate, and the like. In some instances the antibody belongs to a sub-type that activates serum complement when complexed with the transmembrane protein thereby mediating cytotoxicity. Thus, colorectal cancer is treated by administering to a patient antibodies directed against the transmembrane colorectal cancer protein.

[128] In another preferred embodiment, the antibody is conjugated to a therapeutic moiety. In one aspect the therapeutic moiety is a small molecule that modulates the activity of the colorectal cancer protein. In another aspect the therapeutic moiety modulates the activity of molecules associated with or in close proximity to the colorectal cancer protein. The therapeutic moiety may inhibit enzymatic activity such as protease or protein kinase activity associated with colorectal cancer.

[129] In a preferred embodiment, the therapeutic moiety may also be a cytotoxic agent. In this method, targeting the cytotoxic agent to tumor tissue or cells, results in a reduction in the number of afflicted cells, thereby reducing symptoms associated with colorectal cancer. Cytotoxic agents are numerous and varied and include, but are not limited to, cytotoxic drugs or toxins or active fragments of such toxins. Suitable toxins and their corresponding fragments include diphtheria A chain, exotoxin A chain, ricin A chain, abrin A chain, curcin, crotin, phenomycin, enomycin and the like. Cytotoxic agents also include radiochemicals made by conjugating radioisotopes to antibodies raised against colorectal cancer proteins, or binding of a radionuclide to a chelating agent that has been covalently attached to the antibody. Targeting the therapeutic moiety to transmembrane colorectal cancer proteins not only serves to increase the local concentration of therapeutic moiety in the colorectal cancer afflicted area, but also serves to reduce deleterious side effects that may be associated with the therapeutic moiety.

[130] In another preferred embodiment, the colorectal cancer protein against which the antibodies are raised is an intracellular protein. In this case, the antibody may be conjugated to a protein which facilitates entry into the cell. In one case, the antibody enters the cell by endocytosis. In another embodiment, a nucleic acid encoding the antibody is administered to the individual or cell. Moreover, wherein the colorectal cancer protein can be targeted within a cell, i.e., the nucleus, an antibody thereto contains a signal for that target localization, i.e., a nuclear localization signal.

[131] The colorectal cancer antibodies of the invention specifically bind to colorectal cancer proteins. By "specifically bind" herein is meant that the antibodies bind to the protein with a binding constant in the range of at least 10^{-4} - 10^{-6} M^{-1} , with a preferred range being 10^{-7} - 10^{-9} M^{-1} .

[132] In a preferred embodiment, the colorectal cancer protein is purified or isolated after expression. Colorectal cancer proteins may be isolated or purified in a variety of ways known to those skilled in the art depending on what other components are present in the sample. Standard purification methods include electrophoretic, molecular, immunological and chromatographic techniques, including ion exchange, hydrophobic, affinity, and reverse-phase HPLC chromatography, and chromatofocusing. For example, the colorectal cancer protein may be purified using a standard anti-colorectal cancer antibody column. Ultrafiltration and diafiltration techniques, in conjunction with protein concentration, are also useful. For general guidance in suitable purification techniques, see Scopes, R., Protein Purification, Springer-Verlag, NY (1982). The degree of purification necessary will vary depending on the use of the colorectal cancer protein. In some instances no purification will be necessary.

[133] Once expressed and purified if necessary, the colorectal cancer proteins and nucleic acids are useful in a number of applications.

[134] In one aspect, the expression levels of genes are determined for different cellular states in the colorectal cancer phenotype; that is, the expression levels of genes in normal colon tissue and in colorectal cancer tissue (and in some cases, for varying severities of colorectal cancer that relate to prognosis, as outlined below) are evaluated to provide expression profiles. An expression profile of a particular cell state or point of development is essentially a "fingerprint" of the state; while two states may have any particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is unique to the state of the cell. By comparing expression profiles of cells in different states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. Then, diagnosis may be done or confirmed: does tissue from a particular patient have the gene expression profile of normal or colorectal cancer tissue.

[01] "Differential expression," or grammatical equivalents as used herein, refers to both qualitative as well as quantitative differences in the genes' temporal and/or cellular expression patterns within and among the cells. Thus, a differentially expressed gene can qualitatively have its expression altered, including an activation or inactivation, in, for example, normal versus colorectal cancer tissue. That is, genes may be turned on or turned off in a particular state, relative to another state. As is apparent to the skilled artisan, any comparison of two or more states can be made. Such a qualitatively regulated gene will exhibit an expression pattern within a state or cell type which is detectable by standard

techniques in one such state or cell type, but is not detectable in both. Alternatively, the determination is quantitative in that expression is increased or decreased; that is, the expression of the gene is either upregulated, resulting in an increased amount of transcript, or downregulated, resulting in a decreased amount of transcript. The degree to which expression differs need only be large enough to quantify via standard characterization techniques as outlined below, such as by use of Affymetrix GeneChip™ expression arrays, Lockhart, Nature Biotechnology, 14:1675-1680 (1996), hereby expressly incorporated by reference. Other techniques include, but are not limited to, quantitative reverse transcriptase PCR, Northern analysis and RNase protection. As outlined above, preferably the change in expression (i.e. upregulation or downregulation) is at least about 50%, more preferably at least about 100%, more preferably at least about 150%, more preferably, at least about 200%, with from 300 to at least 1000% being especially preferred.

[136] As will be appreciated by those in the art, this may be done by evaluation at either the gene transcript, or the protein level; that is, the amount of gene expression may be monitored using nucleic acid probes to the DNA or RNA equivalent of the gene transcript, and the quantification of gene expression levels, or, alternatively, the final gene product itself (protein) can be monitored, for example through the use of antibodies to the colorectal cancer protein and standard immunoassays (ELISAs, etc.) or other techniques, including mass spectroscopy assays, 2D gel electrophoresis assays, etc. Thus, the proteins corresponding to colorectal cancer genes, i.e. those identified as being important in a colorectal cancer phenotype, can be evaluated in a colorectal cancer diagnostic test.

[137] In a preferred embodiment, gene expression monitoring is done and a number of genes, i.e. an expression profile, is monitored simultaneously, although multiple protein expression monitoring can be done as well. Similarly, these assays may be done on an individual basis as well.

[138] In this embodiment, the colorectal cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of colorectal cancer sequences in a particular cell. The assays are further described below in the example.

[139] In a preferred embodiment nucleic acids encoding the colorectal cancer protein are detected. Although DNA or RNA encoding the colorectal cancer protein may be detected, of particular interest are methods wherein the mRNA encoding a colorectal cancer protein is detected. The presence of mRNA in a sample is an indication that the colorectal cancer gene has been transcribed to form the mRNA, and suggests that the protein

is expressed. Probes to detect the mRNA can be any nucleotide/deoxynucleotide probe that is complementary to and base pairs with the mRNA and includes but is not limited to oligonucleotides, cDNA or RNA. Probes also should contain a detectable label, as defined herein. In one method the mRNA is detected after immobilizing the nucleic acid to be examined on a solid support such as nylon membranes and hybridizing the probe with the sample. Following washing to remove the non-specifically bound probe, the label is detected. In another method detection of the mRNA is performed in situ. In this method permeabilized cells or tissue samples are contacted with a detectably labeled nucleic acid probe for sufficient time to allow the probe to hybridize with the target mRNA. Following washing to remove the non-specifically bound probe, the label is detected. For example a digoxigenin labeled riboprobe (RNA probe) that is complementary to the mRNA encoding a colorectal cancer protein is detected by binding the digoxigenin with an anti-digoxigenin secondary antibody and developed with nitro blue tetrazolium and 5-bromo-4-chloro-3-indoyl phosphate.

[140] In a preferred embodiment, any of the three classes of proteins as described herein (secreted, transmembrane or intracellular proteins) are used in diagnostic assays. The colorectal cancer proteins, antibodies, nucleic acids, modified proteins and cells containing colorectal cancer sequences are used in diagnostic assays. This can be done on an individual gene or corresponding polypeptide level. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes and/or corresponding polypeptides.

[141] As described and defined herein, colorectal cancer proteins, including intracellular, transmembrane or secreted proteins, find use as markers of colorectal cancer.

Detection of these proteins in putative colorectal cancer tissue or patients allows for a determination or diagnosis of colorectal cancer. Numerous methods known to those of ordinary skill in the art find use in detecting colorectal cancer. In one embodiment, antibodies are used to detect colorectal cancer proteins. A preferred method separates proteins from a sample or patient by electrophoresis on a gel (typically a denaturing and reducing protein gel, but may be any other type of gel including isoelectric focusing gels and the like). Following separation of proteins, the colorectal cancer protein is detected by immunoblotting with antibodies raised against the colorectal cancer protein. Methods of immunoblotting are well known to those of ordinary skill in the art.

[142] In another preferred method, antibodies to the colorectal cancer protein find use in in situ imaging techniques. In this method cells are contacted with from one to many antibodies to the colorectal cancer protein(s). Following washing to remove non-specific antibody binding, the presence of the antibody or antibodies is detected. In one embodiment the antibody is detected by incubating with a secondary antibody that contains a detectable label. In another method the primary antibody to the colorectal cancer protein(s) contains a detectable label. In another preferred embodiment each one of multiple primary antibodies contains a distinct and detectable label. This method finds particular use in simultaneous screening for a plurality of colorectal cancer proteins. As will be appreciated by one of ordinary skill in the art, numerous other histological imaging techniques are useful in the invention.

[143] In a preferred embodiment the label is detected in a fluorometer which has the ability to detect and distinguish emissions of different wavelengths. In addition, a fluorescence activated cell sorter (FACS) can be used in the method.

[144] In another preferred embodiment, antibodies find use in diagnosing colorectal cancer from blood samples. As previously described, certain colorectal cancer proteins are secreted/circulating molecules. Blood samples, therefore, are useful as samples to be probed or tested for the presence of secreted colorectal cancer proteins. Antibodies can be used to detect the colorectal cancer by any of the previously described immunoassay techniques including ELISA, immunoblotting (Western blotting), immunoprecipitation, BIACORE technology and the like, as will be appreciated by one of ordinary skill in the art.

[145] In a preferred embodiment, in situ hybridization of labeled colorectal cancer nucleic acid probes to tissue arrays is done. For example, arrays of tissue samples, including colorectal cancer tissue and/or normal tissue, are made. In situ hybridization as is known in the art can then be done.

[146] It is understood that when comparing the fingerprints between an individual and a standard, the skilled artisan can make a diagnosis as well as a prognosis. It is further understood that the genes which indicate the diagnosis may differ from those which indicate the prognosis.

[147] In a preferred embodiment, the colorectal cancer proteins, antibodies, nucleic acids, modified proteins and cells containing colorectal cancer sequences are used in prognosis assays. As above, gene expression profiles can be generated that correlate to colorectal cancer severity, in terms of long term prognosis. Again, this may be done on either a protein or gene level, with the use of genes being preferred. As above, the colorectal

cancer probes are attached to biochips for the detection and quantification of colorectal cancer sequences in a tissue or patient. The assays proceed as outlined for diagnosis.

[148] In a preferred embodiment, any of the three classes of proteins as described herein are used in drug screening assays. The colorectal cancer proteins, antibodies, nucleic acids, modified proteins and cells containing colorectal cancer sequences are used in drug screening assays or by evaluating the effect of drug candidates on a "gene expression profile" or expression profile of polypeptides. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent, Zlokarnik, et al., Science 279, 84-8 (1998), Heid, 1996 #69.

[149] In a preferred embodiment, the colorectal cancer proteins, antibodies, nucleic acids, modified proteins and cells containing the native or modified colorectal cancer proteins are used in screening assays. That is, the present invention provides novel methods for screening for compositions which modulate the colorectal cancer phenotype. As above, this can be done on an individual gene level or by evaluating the effect of drug candidates on a "gene expression profile". In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent, see Zlokarnik, supra.

[150] Having identified the differentially expressed genes herein, a variety of assays may be executed. In a preferred embodiment, assays may be run on an individual gene or protein level. That is, having identified a particular gene as up regulated in colorectal cancer, candidate bioactive agents may be screened to modulate this gene's response; preferably to down regulate the gene, although in some circumstances to up regulate the gene. "Modulation" thus includes both an increase and a decrease in gene expression. The preferred amount of modulation will depend on the original change of the gene expression in normal versus tumor tissue, with changes of at least 10%, preferably 50%, more preferably 100-300%, and in some embodiments 300-1000% or greater. Thus, if a gene exhibits a 4 fold increase in tumor compared to normal tissue, a decrease of about four fold is desired; a 10 fold decrease in tumor compared to normal tissue gives a 10 fold increase in expression for a candidate agent is desired.

[151] As will be appreciated by those in the art, this may be done by evaluation at either the gene or the protein level; that is, the amount of gene expression may be monitored using nucleic acid probes and the quantification of gene expression levels, or,

alternatively, the gene product itself can be monitored, for example through the use of antibodies to the colorectal cancer protein and standard immunoassays.

[152] In a preferred embodiment, gene expression monitoring is done and a number of genes, i.e. an expression profile, is monitored simultaneously, although multiple protein expression monitoring can be done as well.

[153] In this embodiment, the colorectal cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of colorectal cancer sequences in a particular cell. The assays are further described below.

[154] Generally, in a preferred embodiment, a candidate bioactive agent is added to the cells prior to analysis. Moreover, screens are provided to identify a candidate bioactive agent which modulates colorectal cancer, modulates colorectal cancer proteins, binds to a colorectal cancer protein, or interferes between the binding of a colorectal cancer protein and an antibody.

[155] The term "candidate bioactive agent" or "drug candidate" or grammatical equivalents as used herein describes any molecule, e.g., protein, oligopeptide, small organic molecule, polysaccharide, polynucleotide, etc., to be tested for bioactive agents that are capable of directly or indirectly altering either the colorectal cancer phenotype or the expression of a colorectal cancer sequence, including both nucleic acid sequences and protein sequences. In preferred embodiments, the bioactive agents modulate the expression profiles, or expression profile nucleic acids or proteins provided herein. In a particularly preferred embodiment, the candidate agent suppresses a colorectal cancer phenotype, for example to a normal colon tissue fingerprint. Similarly, the candidate agent preferably suppresses a severe colorectal cancer phenotype. Generally a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a differential response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e., at zero concentration or below the level of detection.

[156] In one aspect, a candidate agent will neutralize the effect of a colorectal cancer protein. By "neutralize" is meant that activity of a protein is either inhibited or counter acted against so as to have substantially no effect on a cell.

[157] Candidate agents encompass numerous chemical classes, though typically they are organic molecules, preferably small organic compounds having a molecular weight of more than 100 and less than about 2,500 daltons. Preferred small molecules are less than 2000, or less than 1500 or less than 1000 or less than 500 D. Candidate agents comprise functional groups necessary for structural interaction with proteins, particularly

hydrogen bonding, and typically include at least an amine, carbonyl, hydroxyl or carboxyl group, preferably at least two of the functional chemical groups. The candidate agents often comprise cyclical carbon or heterocyclic structures and/or aromatic or polyaromatic structures substituted with one or more of the above functional groups. Candidate agents are also found among biomolecules including peptides, saccharides, fatty acids, steroids, purines, pyrimidines, derivatives, structural analogs or combinations thereof. Particularly preferred are peptides.

[158] Candidate agents are obtained from a wide variety of sources including libraries of synthetic or natural compounds. For example, numerous means are available for random and directed synthesis of a wide variety of organic compounds and biomolecules, including expression of randomized oligonucleotides. Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant and animal extracts are available or readily produced. Additionally, natural or synthetically produced libraries and compounds are readily modified through conventional chemical, physical and biochemical means. Known pharmacological agents may be subjected to directed or random chemical modifications, such as acylation, alkylation, esterification, amidification to produce structural analogs.

[159] In a preferred embodiment, the candidate bioactive agents are proteins. By "protein" herein is meant at least two covalently attached amino acids, which includes proteins, polypeptides, oligopeptides and peptides. The protein may be made up of naturally occurring amino acids and peptide bonds, or synthetic peptidomimetic structures. Thus "amino acid", or "peptide residue", as used herein means both naturally occurring and synthetic amino acids. For example, homo-phenylalanine, citrulline and noreleucine are considered amino acids for the purposes of the invention. "Amino acid" also includes imino acid residues such as proline and hydroxyproline. The side chains may be in either the (R) or the (S) configuration. In the preferred embodiment, the amino acids are in the (S) or L-configuration. If non-naturally occurring side chains are used, non-amino acid substituents may be used, for example to prevent or retard in vivo degradations.

[160] In a preferred embodiment, the candidate bioactive agents are naturally occurring proteins or fragments of naturally occurring proteins. Thus, for example, cellular extracts containing proteins, or random or directed digests of proteinaceous cellular extracts, may be used. In this way libraries of procaryotic and eucaryotic proteins may be made for screening in the methods of the invention. Particularly preferred in this embodiment are libraries of bacterial, fungal, viral, and mammalian proteins, with the latter being preferred, and human proteins being especially preferred.

[161] In a preferred embodiment, the candidate bioactive agents are peptides of from about 5 to about 30 amino acids, with from about 5 to about 20 amino acids being preferred, and from about 7 to about 15 being particularly preferred. The peptides may be digests of naturally occurring proteins as is outlined above, random peptides, or "biased" random peptides. By "randomized" or grammatical equivalents herein is meant that each nucleic acid and peptide consists of essentially random nucleotides and amino acids, respectively. Since generally these random peptides (or nucleic acids, discussed below) are chemically synthesized, they may incorporate any nucleotide or amino acid at any position. The synthetic process can be designed to generate randomized proteins or nucleic acids, to allow the formation of all or most of the possible combinations over the length of the sequence, thus forming a library of randomized candidate bioactive proteinaceous agents.

[162] In one embodiment, the library is fully randomized, with no sequence preferences or constants at any position. In a preferred embodiment, the library is biased. That is, some positions within the sequence are either held constant, or are selected from a limited number of possibilities. For example, in a preferred embodiment, the nucleotides or amino acid residues are randomized within a defined class, for example, of hydrophobic amino acids, hydrophilic residues, sterically biased (either small or large) residues, towards the creation of nucleic acid binding domains, the creation of cysteines, for cross-linking, prolines for SH-3 domains, serines, threonines, tyrosines or histidines for phosphorylation sites, etc., or to purines, etc.

[163] In a preferred embodiment, the candidate bioactive agents are nucleic acids, as defined above.

[164] As described above generally for proteins, nucleic acid candidate bioactive agents may be naturally occurring nucleic acids, random nucleic acids, or "biased" random nucleic acids. For example, digests of procaryotic or eucaryotic genomes may be used as is outlined above for proteins.

[165] In a preferred embodiment, the candidate bioactive agents are organic chemical moieties, a wide variety of which are available in the literature.

[166] After the candidate agent has been added and the cells allowed to incubate for some period of time, the sample containing the target sequences to be analyzed is added to the biochip. If required, the target sequence is prepared using known techniques. For example, the sample may be treated to lyse the cells, using known lysis buffers, electroporation, etc., with purification and/or amplification such as PCR occurring as needed, as will be appreciated by those in the art. For example, an in vitro transcription with labels

covalently attached to the nucleosides is done. Generally, the nucleic acids are labeled with biotin-FTTC or PE, or with cy3 or cy5.

[167] In a preferred embodiment, the target sequence is labeled with, for example, a fluorescent, a chemiluminescent, a chemical, or a radioactive signal, to provide a means of detecting the target sequence's specific binding to a probe. The label also can be an enzyme, such as, alkaline phosphatase or horseradish peroxidase, which when provided with an appropriate substrate produces a product that can be detected. Alternatively, the label can be a labeled compound or small molecule, such as an enzyme inhibitor, that binds but is not catalyzed or altered by the enzyme. The label also can be a moiety or compound, such as, an epitope tag or biotin which specifically binds to streptavidin. For the example of biotin, the streptavidin is labeled as described above, thereby, providing a detectable signal for the bound target sequence. As known in the art, unbound labeled streptavidin is removed prior to analysis.

[168] As will be appreciated by those in the art, these assays can be direct hybridization assays or can comprise "sandwich assays", which include the use of multiple probes, as is generally outlined in U.S. Patent Nos. 5,681,702, 5,597,909, 5,545,730, 5,594,117, 5,591,584, 5,571,670, 5,580,731, 5,571,670, 5,591,584, 5,624,802, 5,635,352, 5,594,118, 5,359,100, 5,124,246 and 5,681,697, all of which are hereby incorporated by reference. In this embodiment, in general, the target nucleic acid is prepared as outlined above, and then added to the biochip comprising a plurality of nucleic acid probes, under conditions that allow the formation of a hybridization complex.

[169] A variety of hybridization conditions may be used in the present invention, including high, moderate and low stringency conditions as outlined above. The assays are generally run under stringency conditions which allows formation of the label probe hybridization complex only in the presence of target. Stringency can be controlled by altering a step parameter that is a thermodynamic variable, including, but not limited to, temperature, formamide concentration, salt concentration, chaotropic salt concentration pH, organic solvent concentration, etc.

[170] These parameters may also be used to control non-specific binding, as is generally outlined in U.S. Patent No. 5,681,697. Thus it may be desirable to perform certain steps at higher stringency conditions to reduce non-specific binding.

[171] The reactions outlined herein may be accomplished in a variety of ways, as will be appreciated by those in the art. Components of the reaction may be added simultaneously, or sequentially, in any order, with preferred embodiments outlined below. In

addition, the reaction may include a variety of other reagents may be included in the assays. These include reagents like salts, buffers, neutral proteins, e.g. albumin, detergents, etc which may be used to facilitate optimal hybridization and detection, and/or reduce non-specific or background interactions. Also reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may be used, depending on the sample preparation methods and purity of the target.

[172] Once the assay is run, the data is analyzed to determine the expression levels, and changes in expression levels as between states, of individual genes, forming a gene expression profile.

[173] The screens are done to identify drugs or bioactive agents that modulate the colorectal cancer phenotype. Specifically, there are several types of screens that can be run. A preferred embodiment is in the screening of candidate agents that can induce or suppress a particular expression profile, thus preferably generating the associated phenotype. That is, candidate agents that can mimic or produce an expression profile in colorectal cancer similar to the expression profile of normal colon tissue is expected to result in a suppression of the colorectal cancer phenotype. Thus, in this embodiment, mimicking an expression profile, or changing one profile to another, is the goal.

[174] In a preferred embodiment, as for the diagnosis and prognosis applications, having identified the differentially expressed genes important in any one state, screens can be run to alter the expression of the genes individually. That is, screening for modulation of regulation of expression of a single gene can be done; that is, rather than try to mimic all or part of an expression profile, screening for regulation of individual genes can be done. Thus, for example, particularly in the case of target genes whose presence or absence is unique between two states, screening is done for modulators of the target gene expression.

[175] In a preferred embodiment, screening is done to alter the biological function of the expression product of the differentially expressed gene. Again, having identified the importance of a gene in a particular state, screening for agents that bind and/or modulate the biological activity of the gene product can be run as is more fully outlined below.

[176] Thus, screening of candidate agents that modulate the colorectal cancer phenotype either at the gene expression level or the protein level can be done.

[177] In addition screens can be done for novel genes that are induced in response to a candidate agent. After identifying a candidate agent based upon its ability to suppress a colorectal cancer expression pattern leading to a normal expression pattern, or

modulate a single colorectal cancer gene expression profile so as to mimic the expression of the gene from normal tissue, a screen as described above can be performed to identify genes that are specifically modulated in response to the agent. Comparing expression profiles between normal tissue and agent treated colorectal cancer tissue reveals genes that are not expressed in normal tissue or colorectal cancer tissue, but are expressed in agent treated tissue. These agent specific sequences can be identified and used by any of the methods described herein for colorectal cancer genes or proteins. In particular these sequences and the proteins they encode find use in marking or identifying agent treated cells. In addition, antibodies can be raised against the agent induced proteins and used to target novel therapeutics to the treated colorectal cancer tissue sample.

[178] Thus, in one embodiment, a candidate agent is administered to a population of colorectal cancer cells, that thus has an associated colorectal cancer expression profile. By "administration" or "contacting" herein is meant that the candidate agent is added to the cells in such a manner as to allow the agent to act upon the cell, whether by uptake and intracellular action, or by action at the cell surface. In some embodiments, nucleic acid encoding a proteinaceous candidate agent (i.e. a peptide) may be put into a viral construct such as a retroviral construct and added to the cell, such that expression of the peptide agent is accomplished; see PCT US97/01019, hereby expressly incorporated by reference.

[179] Once the candidate agent has been administered to the cells, the cells can be washed if desired and are allowed to incubate under preferably physiological conditions for some period of time. The cells are then harvested and a new gene expression profile is generated, as outlined herein.

[180] Thus, for example, colorectal cancer tissue may be screened for agents that reduce or suppress the colorectal cancer phenotype. A change in at least one gene of the expression profile indicates that the agent has an effect on colorectal cancer activity. By defining such a signature for the colorectal cancer phenotype, screens for new drugs that alter the phenotype can be devised. With this approach, the drug target need not be known and need not be represented in the original expression screening platform, nor does the level of transcript for the target protein need to change.

[181] In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of either the expression of the gene or the gene product itself can be done. The gene products of

differentially expressed genes are sometimes referred to herein as "colorectal cancer modulator proteins". The colorectal cancer modulator protein may be a fragment, or alternatively, be the full length protein to a fragment shown herein. Preferably, the colorectal cancer modulator protein is a fragment of approximately 14 to 24 amino acids long. More preferably the fragment is a soluble fragment.

[182] In a preferred embodiment, the fragment is charged and from the c-terminus. In one embodiment, the c-terminus of the fragment is kept as a free acid and the n-terminus is a free amine to aid in coupling, i.e., to cysteine. In another embodiment, the fragment is an internal peptide overlapping hydrophilic stretch the protein. In a preferred embodiment, the termini is blocked. In another preferred embodiment, the fragment is a novel fragment from the N-terminal. In one embodiment, the fragment excludes sequence outside of the N-terminal, in another embodiment, the fragment includes at least a portion of the N-terminal. "N-terminal" is used interchangeably herein with "N-terminus" which is further described above.

[183] In one embodiment the colorectal cancer proteins are conjugated to an immunogenic agent as discussed herein. In one embodiment the colorectal cancer protein is conjugated to BSA.

[184] Thus, in a preferred embodiment, screening for modulators of expression of specific genes can be done. This will be done as outlined above, but in general the expression of only one or a few genes are evaluated.

[185] In a preferred embodiment, screens are designed to first find candidate agents that can bind to differentially expressed proteins, and then these agents may be used in assays that evaluate the ability of the candidate agent to modulate differentially expressed activity. Thus, as will be appreciated by those in the art, there are a number of different assays which may be run; binding assays and activity assays.

[186] In a preferred embodiment, binding assays are done. In general, purified or isolated gene product is used; that is, the gene products of one or more differentially expressed nucleic acids are made. In general, this is done as is known in the art. For example, antibodies are generated to the protein gene products, and standard immunoassays are run to determine the amount of protein present. Alternatively, cells comprising the colorectal cancer proteins can be used in the assays.

[187] Thus, in a preferred embodiment, the methods comprise combining a colorectal cancer protein and a candidate bioactive agent, and determining the binding of the candidate agent to the colorectal cancer protein. Preferred embodiments utilize the human

colorectal cancer protein, although other mammalian proteins may also be used, for example for the development of animal models of human disease. In some embodiments, as outlined herein, variant or derivative colorectal cancer proteins may be used.

[188] Generally, in a preferred embodiment of the methods herein, the colorectal cancer protein or the candidate agent is non-diffusably bound to an insoluble support having isolated sample receiving areas (e.g. a microtiter plate, an array, etc.). The insoluble supports may be made of any composition to which the compositions can be bound, is readily separated from soluble material, and is otherwise compatible with the overall method of screening. The surface of such supports may be solid or porous and of any convenient shape. Examples of suitable insoluble supports include microtiter plates, arrays, membranes and beads. These are typically made of glass, plastic (e.g., polystyrene), polysaccharides, nylon or nitrocellulose, teflon, etc. Microtiter plates and arrays are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. The particular manner of binding of the composition is not crucial so long as it is compatible with the reagents and overall methods of the invention, maintains the activity of the composition and is nondiffusable. Preferred methods of binding include the use of antibodies (which do not sterically block either the ligand binding site or activation sequence when the protein is bound to the support), direct binding to "sticky" or ionic supports, chemical crosslinking, the synthesis of the protein or agent on the surface, etc. Following binding of the protein or agent, excess unbound material is removed by washing. The sample receiving areas may then be blocked through incubation with bovine serum albumin (BSA), casein or other innocuous protein or other moiety.

[189] In a preferred embodiment, the colorectal cancer protein is bound to the support, and a candidate bioactive agent is added to the assay. Alternatively, the candidate agent is bound to the support and the colorectal cancer protein is added. Novel binding agents include specific antibodies, non-natural binding agents identified in screens of chemical libraries, peptide analogs, etc. Of particular interest are screening assays for agents that have a low toxicity for human cells. A wide variety of assays may be used for this purpose, including labeled in vitro protein-protein binding assays, electrophoretic mobility shift assays, immunoassays for protein binding, functional assays (phosphorylation assays, etc.) and the like.

[190] The determination of the binding of the candidate bioactive agent to the colorectal cancer protein may be done in a number of ways. In a preferred embodiment, the candidate bioactive agent is labeled, and binding determined directly. For example, this

may be done by attaching all or a portion of the colorectal cancer protein to a solid support, adding a labeled candidate agent (for example a fluorescent label), washing off excess reagent, and determining whether the label is present on the solid support. Various blocking and washing steps may be utilized as is known in the art.

5 [191] By "labeled" herein is meant that the compound is either directly or indirectly labeled with a label which provides a detectable signal, e.g. radioisotope, fluorescers, enzyme, antibodies, particles such as magnetic particles, chemiluminescers, or specific binding molecules, etc. Specific binding molecules include pairs, such as biotin and streptavidin, digoxin and antidigoxin etc. For the specific binding members, the
10 complementary member would normally be labeled with a molecule which provides for detection, in accordance with known procedures, as outlined above. The label can directly or indirectly provide a detectable signal.

15 [192] In some embodiments, only one of the components is labeled. For example, the proteins (or proteinaceous candidate agents) may be labeled at tyrosine positions using ^{125}I , or with fluorophores. Alternatively, more than one component may be labeled with different labels; using ^{125}I for the proteins, for example, and a fluorophor for the candidate agents.

20 [193] In a preferred embodiment, the binding of the candidate bioactive agent is determined through the use of competitive binding assays. In this embodiment, the competitor is a binding moiety known to bind to the target molecule (i.e. colorectal cancer), such as an antibody, peptide, binding partner, ligand, etc. Under certain circumstances, there may be competitive binding as between the bioactive agent and the binding moiety, with the binding moiety displacing the bioactive agent.

25 [194] In one embodiment, the candidate bioactive agent is labeled. Either the candidate bioactive agent, or the competitor, or both, is added first to the protein for a time sufficient to allow binding, if present. Incubations may be performed at any temperature which facilitates optimal activity, typically between 4 and 40°C. Incubation periods are selected for optimum activity, but may also be optimized to facilitate rapid high through put screening. Typically between 0.1 and 1 hour will be sufficient. Excess reagent is
30 generally removed or washed away. The second component is then added, and the presence or absence of the labeled component is followed, to indicate binding.

 [195] In a preferred embodiment, the competitor is added first, followed by the candidate bioactive agent. Displacement of the competitor is an indication that the candidate bioactive agent is binding to the colorectal cancer protein and thus is capable of

binding to, and potentially modulating, the activity of the colorectal cancer protein. In this embodiment, either component can be labeled. Thus, for example, if the competitor is labeled, the presence of label in the wash solution indicates displacement by the agent. Alternatively, if the candidate bioactive agent is labeled, the presence of the label on the support indicates displacement.

[196] In an alternative embodiment, the candidate bioactive agent is added first, with incubation and washing, followed by the competitor. The absence of binding by the competitor may indicate that the bioactive agent is bound to the colorectal cancer protein with a higher affinity. Thus, if the candidate bioactive agent is labeled, the presence of the label on the support, coupled with a lack of competitor binding, may indicate that the candidate agent is capable of binding to the colorectal cancer protein.

[197] In a preferred embodiment, the methods comprise differential screening to identify bioactive agents that are capable of modulating the activity of the colorectal cancer proteins. In this embodiment, the methods comprise combining a colorectal cancer protein and a competitor in a first sample. A second sample comprises a candidate bioactive agent, a colorectal cancer protein and a competitor. The binding of the competitor is determined for both samples, and a change, or difference in binding between the two samples indicates the presence of an agent capable of binding to the colorectal cancer protein and potentially modulating its activity. That is, if the binding of the competitor is different in the second sample relative to the first sample, the agent is capable of binding to the colorectal cancer protein.

[198] Alternatively, a preferred embodiment utilizes differential screening to identify drug candidates that bind to the native colorectal cancer protein, but cannot bind to modified colorectal cancer proteins. The structure of the colorectal cancer protein may be modeled, and used in rational drug design to synthesize agents that interact with that site. Drug candidates that affect colorectal cancer bioactivity are also identified by screening drugs for the ability to either enhance or reduce the activity of the protein.

[199] Positive controls and negative controls may be used in the assays. Preferably all control and test samples are performed in at least triplicate to obtain statistically significant results. Incubation of all samples is for a time sufficient for the binding of the agent to the protein. Following incubation, all samples are washed free of non-specifically bound material and the amount of bound, generally labeled agent determined. For example, where a radiolabel is employed, the samples may be counted in a scintillation counter to determine the amount of bound compound.

[200] A variety of other reagents may be included in the screening assays.

These include reagents like salts, neutral proteins, e.g. albumin, detergents, etc which may be used to facilitate optimal protein-protein binding and/or reduce non-specific or background interactions. Also reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may be used. The mixture of components may be added in any order that provides for the requisite binding.

[201] Screening for agents that modulate the activity of colorectal cancer proteins may also be done. In a preferred embodiment, methods for screening for a bioactive agent capable of modulating the activity of colorectal cancer proteins comprise the steps of adding a candidate bioactive agent to a sample of colorectal cancer proteins, as above, and determining an alteration in the biological activity of colorectal cancer proteins.

"Modulating the activity of colorectal cancer " includes an increase in activity, a decrease in activity, or a change in the type or kind of activity present. Thus, in this embodiment, the candidate agent should both bind to colorectal cancer proteins (although this may not be necessary), and alter its biological or biochemical activity as defined herein. The methods include both in vitro screening methods, as are generally outlined above, and in vivo screening of cells for alterations in the presence, distribution, activity or amount of colorectal cancer proteins.

[202] Thus, in this embodiment, the methods comprise combining a colorectal cancer sample and a candidate bioactive agent, and evaluating the effect on colorectal cancer activity. By "colorectal cancer activity" or grammatical equivalents herein is meant one of the colorectal cancer's biological activities, including, but not limited to, cell division, preferably in colon tissue, cell proliferation, tumor growth, transformation of cells. In one embodiment, colorectal cancer activity includes activation of a gene identified by a nucleic acid of Table 1. An inhibitor of colorectal cancer activity is the inhibition of any one or more colorectal cancer activities.

[203] In a preferred embodiment, the activity of the colorectal cancer protein is increased; in another preferred embodiment, the activity of the colorectal cancer protein is decreased. Thus, bioactive agents that are antagonists are preferred in some embodiments, and bioactive agents that are agonists may be preferred in other embodiments.

[204] In a preferred embodiment, the invention provides methods for screening for bioactive agents capable of modulating the activity of a colorectal cancer protein. The methods comprise adding a candidate bioactive agent, as defined above, to a cell comprising colorectal cancer proteins. Preferred cell types include almost any cell. The

cells contain a recombinant nucleic acid that encodes a colorectal cancer protein. In a preferred embodiment, a library of candidate agents are tested on a plurality of cells.

[205] In one aspect, the assays are evaluated in the presence or absence or previous or subsequent exposure of physiological signals, for example hormones, antibodies, peptides, antigens, cytokines, growth factors, action potentials, pharmacological agents including chemotherapeutics, radiation, carcinogenics, or other cells (i.e. cell-cell contacts). In another example, the determinations are determined at different stages of the cell cycle process.

[206] In this way, bioactive agents are identified. Compounds with pharmacological activity are able to enhance or interfere with the activity of the colorectal cancer protein. In one embodiment, "colorectal cancer protein activity" as used herein includes at least one of the following: colorectal cancer activity, binding to the colorectal cancer protein, activation of the colorectal cancer protein or activation of substrates of the colorectal cancer protein by the colorectal cancer protein. In one embodiment, colorectal cancer activity is defined as the unregulated proliferation of colon tissue, or the growth of cancer in colon tissue. In one aspect, colorectal cancer activity as defined herein is related to the activity of the colorectal cancer protein in the upregulation of the colorectal cancer protein in colon cancer tissue.

[207] In another embodiment, colorectal cancer protein activity includes at least one of the following: colorectal cancer activity, binding to the CBF9 nucleic acid or poly peptide of Table 2 or binding to a nucleic acid of Table 1, or a peptide encoded by a nucleic acid of Table 1 or activation of substrates of the gene products identified by a nucleic acid of Table 1 or substrates of CBF9, which is shown in Table 2. In one aspect, colorectal cancer activity as defined herein is related to the activity of genes defined by the nucleic acids of Table 1 or of CBF9 as defined in Table 2, in colon cancer tissue.

[208] In one embodiment, a method of inhibiting colon cancer cell division is provided. The method comprises administration of a colorectal cancer inhibitor.

[209] In another embodiment, a method of inhibiting tumor growth is provided. The method comprises administration of a colorectal cancer inhibitor.

[210] In a further embodiment, methods of treating cells or individuals with cancer are provided. The method comprises administration of a colorectal cancer inhibitor.

[211] In one embodiment, a colorectal cancer inhibitor is an antibody as discussed above. In another embodiment, the colorectal cancer inhibitor is an antisense molecule. Antisense molecules as used herein include antisense or sense oligonucleotides

comprising a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target mRNA (sense) or DNA (antisense) sequences for colorectal cancer molecules. A preferred antisense molecule is for the colorectal cancer sequences referenced in Table 1 or Table 2, or for a ligand or activator thereof. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment generally at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and Cohen (Cancer Res. 48:2659, 1988) and van der Krol et al. (BioTechniques 6:958, 1988).

[212] Antisense molecules may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell. Alternatively, a sense or an antisense oligonucleotide may be introduced into a cell containing the target nucleic acid sequence by formation of an oligonucleotide-lipid complex, as described in WO 90/10448. It is understood that the use of antisense molecules or knock out and knock in models may also be used in screening assays as discussed above, in addition to methods of treatment.

[213] The compounds having the desired pharmacological activity may be administered in a physiologically acceptable carrier to a host, as previously described. The agents may be administered in a variety of ways, orally, parenterally e.g., subcutaneously, intraperitoneally, intravascularly, etc. Depending upon the manner of introduction, the compounds may be formulated in a variety of ways. The concentration of therapeutically active compound in the formulation may vary from about 0.1-100 wt.%. The agents may be administered alone or in combination with other treatments, i.e., radiation.

[214] The pharmaceutical compositions can be prepared in various forms, such as granules, tablets, pills, suppositories, capsules, suspensions, salves, lotions and the like. Pharmaceutical grade organic or inorganic carriers and/or diluents suitable for oral and topical use can be used to make up compositions containing the therapeutically-active compounds. Diluents known to the art include aqueous media, vegetable and animal oils and fats. Stabilizing agents, wetting and emulsifying agents, salts for varying the osmotic

pressure or buffers for securing an adequate pH value, and skin penetration enhancers can be used as auxiliary agents.

[215] Without being bound by theory, it appears that the various colorectal cancer sequences are important in colorectal cancer. Accordingly, disorders based on mutant or variant colorectal cancer genes may be determined. In one embodiment, the invention provides methods for identifying cells containing variant colorectal cancer genes comprising determining all or part of the sequence of at least one endogenous colorectal cancer genes in a cell. As will be appreciated by those in the art, this may be done using any number of sequencing techniques. In a preferred embodiment, the invention provides methods of identifying the colorectal cancer genotype of an individual comprising determining all or part of the sequence of at least one colorectal cancer gene of the individual. This is generally done in at least one tissue of the individual, and may include the evaluation of a number of tissues or different samples of the same tissue. The method may include comparing the sequence of the sequenced colorectal cancer gene to a known colorectal cancer gene, i.e. a wild-type gene.

[216] The sequence of all or part of the colorectal cancer gene can then be compared to the sequence of a known colorectal cancer gene to determine if any differences exist. This can be done using any number of known homology programs, such as Bestfit, etc. In a preferred embodiment, the presence of a difference in the sequence between the colorectal cancer gene of the patient and the known colorectal cancer gene is indicative of a disease state or a propensity for a disease state, as outlined herein.

[217]

[218] In a preferred embodiment, the colorectal cancer genes are used as probes to determine the number of copies of the colorectal cancer gene in the genome.

[219] In another preferred embodiment colorectal cancer genes are used as probed to determine the chromosomal localization of the colorectal cancer genes. Information such as chromosomal localization finds use in providing a diagnosis or prognosis in particular when chromosomal abnormalities such as translocations, and the like are identified in colorectal cancer gene loci.

[220] Thus, in one embodiment, methods of modulating colorectal cancer in cells or organisms are provided. In one embodiment, the methods comprise administering to a cell an anti-colorectal cancer antibody that reduces or eliminates the biological activity of an endogenous colorectal cancer protein. Alternatively, the methods comprise administering to a cell or organism a recombinant nucleic acid encoding a colorectal cancer

protein. As will be appreciated by those in the art, this may be accomplished in any number of ways. In a preferred embodiment, for example when the colorectal cancer sequence is down-regulated in colorectal cancer, the activity of the colorectal cancer gene is increased by increasing the amount of colorectal cancer in the cell, for example by overexpressing the endogenous colorectal cancer or by administering a gene encoding the colorectal cancer sequence, using known gene-therapy techniques, for example. In a preferred embodiment, the gene therapy techniques include the incorporation of the endogenous gene using enhanced homologous recombination (EHR), for example as described in PCT/US93/03868, hereby incorporated by reference in its entirety. Alternatively, for example when the colorectal cancer sequence is up-regulated in colorectal cancer, the activity of the endogenous colorectal cancer gene is decreased, for example by the administration of a colorectal cancer antisense nucleic acid.

[221] In one embodiment, the colorectal cancer proteins of the present invention may be used to generate polyclonal and monoclonal antibodies to colorectal cancer proteins, which are useful as described herein. Similarly, the colorectal cancer proteins can be coupled, using standard technology, to affinity chromatography columns. These columns may then be used to purify colorectal cancer antibodies. In a preferred embodiment, the antibodies are generated to epitopes unique to a colorectal cancer protein; that is, the antibodies show little or no cross-reactivity to other proteins. These antibodies find use in a number of applications. For example, the colorectal cancer antibodies may be coupled to standard affinity chromatography columns and used to purify colorectal cancer proteins. The antibodies may also be used as blocking polypeptides, as outlined above, since they will specifically bind to the colorectal cancer protein.

[222] In one embodiment, a therapeutically effective dose of a colorectal cancer or modulator thereof is administered to a patient. By "therapeutically effective dose" herein is meant a dose that produces the effects for which it is administered. The exact dose will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques. As is known in the art, adjustments for colorectal cancer degradation, systemic versus localized delivery, and rate of new protease synthesis, as well as the age, body weight, general health, sex, diet, time of administration, drug interaction and the severity of the condition may be necessary, and will be ascertainable with routine experimentation by those skilled in the art.

[223] A "patient" for the purposes of the present invention includes both humans and other animals, particularly mammals, and organisms. Thus the methods are

applicable to both human therapy and veterinary applications. In the preferred embodiment the patient is a mammal, and in the most preferred embodiment the patient is human.

[224] The administration of the colorectal cancer proteins and modulators of the present invention can be done in a variety of ways as discussed above, including, but not limited to, orally, subcutaneously, intravenously, intranasally, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, or intraocularly. In some instances, for example, in the treatment of wounds and inflammation, the colorectal cancer proteins and modulators may be directly applied as a solution or spray.

[225] The pharmaceutical compositions of the present invention comprise a colorectal cancer protein in a form suitable for administration to a patient. In the preferred embodiment, the pharmaceutical compositions are in a water soluble form, such as being present as pharmaceutically acceptable salts, which is meant to include both acid and base addition salts. "Pharmaceutically acceptable acid addition salt" refers to those salts that retain the biological effectiveness of the free bases and that are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid and the like. "Pharmaceutically acceptable base addition salts" include those derived from inorganic bases such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

[226] The pharmaceutical compositions may also include one or more of the following: carrier proteins such as serum albumin; buffers; fillers such as microcrystalline cellulose, lactose, corn and other starches; binding agents; sweeteners and other flavoring agents; coloring agents; and polyethylene glycol. Additives are well known in the art, and are used in a variety of formulations.

[227] In a preferred embodiment, colorectal cancer proteins and modulators are administered as therapeutic agents, and can be formulated as outlined above. Similarly,

colorectal cancer genes (including both the full-length sequence, partial sequences, or regulatory sequences of the colorectal cancer coding regions) can be administered in gene therapy applications, as is known in the art. These colorectal cancer genes can include antisense applications, either as gene therapy (i.e. for incorporation into the genome) or as antisense compositions, as will be appreciated by those in the art.

[228] In a preferred embodiment, colorectal cancer genes are administered as DNA vaccines, either single genes or combinations of colorectal cancer genes. Naked DNA vaccines are generally known in the art. Brower, Nature Biotechnology, 16:1304-1305 (1998).

[229] In one embodiment, colorectal cancer genes of the present invention are used as DNA vaccines. Methods for the use of genes as DNA vaccines are well known to one of ordinary skill in the art, and include placing a colorectal cancer gene or portion of a colorectal cancer gene under the control of a promoter for expression in a colorectal cancer patient. The colorectal cancer gene used for DNA vaccines can encode full-length colorectal cancer proteins, but more preferably encodes portions of the colorectal cancer proteins including peptides derived from the colorectal cancer protein. In a preferred embodiment a patient is immunized with a DNA vaccine comprising a plurality of nucleotide sequences derived from a colorectal cancer gene. Similarly, it is possible to immunize a patient with a plurality of colorectal cancer genes or portions thereof as defined herein. Without being bound by theory, expression of the polypeptide encoded by the DNA vaccine, cytotoxic T-cells, helper T-cells and antibodies are induced which recognize and destroy or eliminate cells expressing colorectal cancer proteins.

[230] In a preferred embodiment, the DNA vaccines include a gene encoding an adjuvant molecule with the DNA vaccine. Such adjuvant molecules include cytokines that increase the immunogenic response to the colorectal cancer polypeptide encoded by the DNA vaccine. Additional or alternative adjuvants are known to those of ordinary skill in the art and find use in the invention.

[231] In another preferred embodiment colorectal cancer genes find use in generating animal models of colorectal cancer. As is appreciated by one of ordinary skill in the art, when the colorectal cancer gene identified is repressed or diminished in colorectal cancer tissue, gene therapy technology wherein antisense RNA directed to the colorectal cancer gene will also diminish or repress expression of the gene. An animal generated as such serves as an animal model of colorectal cancer that finds use in screening bioactive drug candidates. Similarly, gene knockout technology, for example as a result of

homologous recombination with an appropriate gene targeting vector, will result in the absence of the colorectal cancer protein. When desired, tissue-specific expression or knockout of the colorectal cancer protein may be necessary.

[232] It is also possible that the colorectal cancer protein is overexpressed in colorectal cancer. As such, transgenic animals can be generated that overexpress the colorectal cancer protein. Depending on the desired expression level, promoters of various strengths can be employed to express the transgene. Also, the number of copies of the integrated transgene can be determined and compared for a determination of the expression level of the transgene. Animals generated by such methods find use as animal models of colorectal cancer and are additionally useful in screening for bioactive molecules to treat colorectal cancer.

EXAMPLES

[233] It is understood that the examples described herein in no way serve to limit the true scope of this invention, but rather are presented for illustrative purposes. All references and sequences of accession numbers cited herein are incorporated by reference in their entirety.

[234] Example 1

Tissue Preparation, Labeling Chips, and Fingerprints

[235] Purify total RNA from tissue using TRIzol Reagent

[236] Estimate tissue weight. Homogenize tissue samples in 1ml of TRIzol per 50mg of tissue using a Polytron 3100 homogenizer. The generator/probe used depends upon the tissue size. A generator that is too large for the amount of tissue to be homogenized will cause a loss of sample and lower RNA yield. Use the 20mm generator for tissue weighing more than 0.6g. If the working volume is greater than 2ml, then homogenize tissue in a 15ml polypropylene tube (Falcon 2059). Fill tube no greater than 10ml.

HOMOGENIZATION

[237] Before using generator, it should have been cleaned after last usage by running it through soapy H₂O and rinsing thoroughly. Run through with EtOH to sterilize. Keep tissue frozen until ready. Add TRIzol directly to frozen tissue then homogenize.

[238] Following homogenization, remove insoluble material from the homogenate by centrifugation at 7500 x g for 15 min. in a Sorvall superspeed or 12,000 x g for 10 min. in an Eppendorf centrifuge at 4oC. Transfer the cleared homogenate to a new tube(s). The samples may be frozen now at -60 to -70oC (and kept for at least one month) or you may continue with the purification.

PHASE SEPARATION

[239] Incubate the homogenized samples for 5 minutes at room temperature.

[240] Add 0.2ml of chloroform per 1ml of TRIzol reagent used in the original homogenization.

[241] Cap tubes securely and shake tubes vigorously by hand (do not vortex) for 15 seconds.

[242] Incubate samples at room temp. for 2-3 minutes. Centrifuge samples at 6500rpm in a Sorvall superspeed for 30 min. at 4oC. (You may spin at up to 12,000 x g for 10 min. but you risk breaking your tubes in the centrifuge.)

RNA PRECIPITATION

[243] Transfer the aqueous phase to a fresh tube. Save the organic phase if isolation of DNA or protein is desired. Add 0.5ml of isopropyl alcohol per 1ml of TRIzol reagent used in the original homogenization. Cap tubes securely and invert to mix. Incubate samples at room temp. for 10 minutes. Centrifuge samples at 6500rpm in Sorvall for 20min. at 4oC.

RNA WASH

[244] Pour off the supernate. Wash pellet with cold 75% ethanol. Use 1ml of 75% ethanol per 1ml of TRIzol reagent used in the initial homogenization. Cap tubes securely and invert several times to loosen pellet. (Do not vortex). Centrifuge at <8000rpm (<7500 x g) for 5 minutes at 4oC.

[245] Pour off the wash. Carefully transfer pellet to an eppendorf tube (let it slide down the tube into the new tube and use a pipet tip to help guide it in if necessary). Depending on the volumes you are working with, you can decide what size tube(s) you want to precipitate the RNA in. When I tried leaving the RNA in the large 15ml tube, it took so long to dry (i.e. it did not dry) that I eventually had to transfer it to a smaller tube. Let pellet

dry in hood. Resuspend RNA in an appropriate volume of DEPC H₂O. Try for 2-5ug/ul.
Take absorbance readings.

5 [246] Purify poly A+ mRNA from total RNA or clean up total RNA with Qiagen's RNeasy kit

[247] Purification of poly A+ mRNA from total RNA. Heat oligotex suspension to 37oC and mix immediately before adding to RNA. Incubate Elution Buffer at 70oC. Warm up 2 x Binding Buffer at 65oC if there is precipitate in the buffer. Mix total RNA with DEPC-treated water, 2 x Binding Buffer, and Oligotex according to Table 2 on page 16 of the Oligotex Handbook. Incubate for 3 minutes at 65oC. Incubate for 10 minutes at room temperature.

15 [248] Centrifuge for 2 minutes at 14,000 to 18,000 g. If centrifuge has a "soft setting," then use it. Remove supernatant without disturbing Oligotex pellet. A little bit of solution can be left behind to reduce the loss of Oligotex. Save sup until certain that satisfactory binding and elution of poly A+ mRNA has occurred.

20 [249] Gently resuspend in Wash Buffer OW2 and pipet onto spin column. Centrifuge the spin column at full speed (soft setting if possible) for 1 minute.

[250] Transfer spin column to a new collection tube and gently resuspend in Wash Buffer OW2 and centrifuge as describe herein.

25 [251] Transfer spin column to a new tube and elute with 20 to 100 ul of preheated (70oC) Elution Buffer. Gently resuspend Oligotex resin by pipetting up and down. Centrifuge as above. Repeat elution with fresh elution buffer or use first eluate to keep the elution volume low.

30 [252] Read absorbance, using diluted Elution Buffer as the blank.

[253] Before proceeding with cDNA synthesis, the mRNA must be precipitated. Some component leftover or in the Elution Buffer from the Oligotex purification procedure will inhibit downstream enzymatic reactions of the mRNA.

Ethanol Precipitation

- [254] Add 0.4 vol. of 7.5 M NH₄OAc + 2.5 vol. of cold 100% ethanol. Precipitate at -20°C 1 hour to overnight (or 20-30 min. at -70°C). Centrifuge at 14,000-16,000 x g for 30 minutes at 4°C. Wash pellet with 0.5ml of 80% ethanol (-20°C) then centrifuge at 14,000-16,000 x g for 5 minutes at room temperature. Repeat 80% ethanol wash. Dry the last bit of ethanol from the pellet in the hood. (Do not speed vacuum). Suspend pellet in DEPC H₂O at 1ug/ul concentration.

Clean up total RNA using Qiagen's RNeasy kit

- [255] Add no more than 100ug to an RNeasy column. Adjust sample to a volume of 100ul with RNase-free water. Add 350ul Buffer RLT then 250ul ethanol (100%) to the sample. Mix by pipetting (do not centrifuge) then apply sample to an RNeasy mini spin column. Centrifuge for 15 sec at >10,000rpm. If concerned about yield, re-apply flowthrough to column and centrifuge again.
- [256] Transfer column to a new 2-ml collection tube. Add 500ul Buffer RPE and centrifuge for 15 sec at >10,000rpm. Discard flowthrough. Add 500ul Buffer RPE and centrifuge for 15 sec at >10,000rpm. Discard flowthrough then centrifuge for 2 min at maximum speed to dry column membrane. Transfer column to a new 1.5-ml collection tube and apply 30-50ul of RNase-free water directly onto column membrane. Centrifuge 1 min at >10,000rpm. Repeat elution.
- [257] Take absorbance reading. If necessary, ethanol precipitate with ammonium acetate and 2.5X volume 100% ethanol.

- [258] Make cDNA using Gibco's "SuperScript Choice System for cDNA Synthesis" kit

First Strand cDNA Synthesis

- [259] Use 5ug of total RNA or 1ug of polyA+ mRNA as starting material. For total RNA, use 2ul of SuperScript RT. For polyA+ mRNA, use 1ul of SuperScript RT. Final volume of first strand synthesis mix is 20ul. RNA must be in a volume no greater than 10ul. Incubate RNA with 1ul of 100pmol T7-T24 oligo for 10 min at 70°C. On ice, add 7 ul of: 4ul 5X 1st Strand Buffer, 2ul of 0.1M DTT, and 1 ul of 10mM dNTP mix. Incubate at 37°C for 2 min then add SuperScript RT
- Incubate at 37°C for 1 hour.
- Second Strand Synthesis

Place 1st strand reactions on ice.

Add: 91ul DEPC H₂O

30ul 5X 2nd Strand Buffer

3ul 10mM dNTP mix

1ul 10U/ul E.coli DNA Ligase

4ul 10U/ul E.coli DNA Polymerase

1ul 2U/ul RNase H

[260] Make the above into a mix if there are more than 2 samples. Mix and

10 incubate 2 hours at 16C.

[261] Add 2ul T4 DNA Polymerase. Incubate 5 min at 16C. Add 10ul of
0.5M EDTA

[262] Clean up cDNA

15 [263] Phenol:Chloroform:Isoamyl Alcohol (25:24:1) purification using
Phase-Lock gel tubes:

[264] Centrifuge PLG tubes for 30 sec at maximum speed. Transfer cDNA
mix to PLG tube. Add equal volume of phenol:chloroform:isamyl alcohol and shake
vigorously (do not vortex). Centrifuge 5 minutes at maximum speed. Transfer top aqueous
20 solution to a new tube. Ethanol precipitate: add 7.5X 5M NH₄OAc and 2.5X volume of
100% ethanol. Centrifuge immediately at room temp. for 20 min, maximum speed. Remove
sup then wash pellet 2X with cold 80% ethanol. Remove as much ethanol wash as possible
then let pellet air dry. Resuspend pellet in 3ul RNase-free water.

25 In vitro Transcription (IVT) and labeling with biotin

Pipet 1.5ul of cDNA into a thin-wall PCR tube.

Make NTP labeling mix:

30 Combine at room temperature: 2ul T7 10xATP (75mM) (Ambion)
2ul T7 10xGTP (75mM) (Ambion)
1.5ul T7 10xCTP (75mM) (Ambion)
1.5ul T7 10xUTP (75mM) (Ambion)
3.75ul 10mM Bio-11-UTP (Boehringer-Mannheim/Roche or Enzo)
3.75ul 10mM Bio-16-CTP (Enzo)

2ul 10x T7 transcription buffer (Ambion)

2ul 10x T7 enzyme mix (Ambion)

[265] Final volume of total reaction is 20ul. Incubate 6 hours at 37C in a

5 PCR machine.

RNeasy clean-up of IVT product

[266] Follow previous instructions for RNeasy columns or refer to Qiagen's RNeasy protocol handbook.

10

[267] cRNA will most likely need to be ethanol precipitated. Resuspend in a volume compatible with the fragmentation step.

Fragmentation

[268] 15 ug of labeled RNA is usually fragmented. Try to minimize the fragmentation reaction volume; a 10 ul volume is recommended but 20 ul is all right. Do not go higher than 20 ul because the magnesium in the fragmentation buffer contributes to precipitation in the hybridization buffer.

15

[269] Fragment RNA by incubation at 94 C for 35 minutes in 1 x
20 Fragmentation buffer.

5 x Fragmentation buffer:

200 mM Tris-acetate, pH 8.1

500 mM KOAc

150 mM MgOAc

25

[270] The labeled RNA transcript can be analyzed before and after fragmentation. Samples can be heated to 65C for 15 minutes and electrophoresed on 1% agarose/TBE gels to get an approximate idea of the transcript size range

30

Hybridization

[271] 200 ul (10ug cRNA) of a hybridization mix is put on the chip. If multiple hybridizations are to be done (such as cycling through a 5 chip set), then it is recommended that an initial hybridization mix of 300 ul or more be made.

Hybridization Mix: fragment labeled RNA (50ng/ul final conc.)

50 pM 948-b control oligo

1.5 pM BioB

5 pM BioC

25 pM BioD

100 pM CRE

0.1mg/ml herring sperm DNA

0.5mg/ml acetylated BSA

to 300 ul with 1xMES hyb. buffer

[272] The instruction manuals for the products used herein are incorporated herein in their entirety.

Labeling Protocol Provided Herein

Hybridization reaction:

Start with non-biotinylated IVT (purified by RNeasy columns)
(see example 1 for steps from tissue to IVT)

IVT antisense RNA; 4 µg: µl

Random Hexamers (1 µg/µl): 4 µl

H₂O: µl

14 µl

- Incubate 70°C, 10 min. Put on ice.

Reverse transcription:

5X First Strand (BRL) buffer: 6 µl

0.1 M DTT: 3 µl

50X dNTP mix: 0.6 µl

H₂O: 2.4 µl

Cy3 or Cy5 dUTP (1mM): 3 µl

SS RT II (BRL): 1 µl

16 µl

- Add to hybridization reaction.
- Incubate 30 min., 42°C.
- Add 1 µl SSII and let go for another hour.

Put on ice.

- 5 - 50X dNTP mix (25mM of cold dATP, dCTP, and dGTP, 10mM of dTTP: 25 µl each of 100mM dATP, dCTP, and dGTP; 10 µl of 100mM dTTP to 15 µl H₂O. dNTPs from Pharmacia)

RNA degradation:

- 10 86 µl H₂O
- Add 1.5 µl 1M NaOH/ 2mM EDTA, incubate at 65°C, 10 min.
- 10 µl 10N NaOH
- 4 µl 50mM EDTA
- U-Con 30
- 15 500 µl TE/sample spin at 7000g for 10 min, save flow through for purification

Qiagen purification:

- suspend u-con recovered material in 500µl buffer PB
 - proceed w/ normal Qiagen protocol
- 20 DNase digest:
- Add 1 µl of 1/100 dil of DNase/30µl Rx and incubate at 37°C for 15 min.
 - 5 min 95°C to denature enzyme

Sample preparation:

- 25 - Add:
- Cot-1 DNA: 10 µl
- 50X dNTPs: 1 µl
- Na pyro phosphate: 7.5 µl
- 10mg/ml Herring sperm DNA 1ul of 1/10 dilution
- 30 21.8 final vol.
- Dry down in speed vac.
 - Resuspend in 15 µl H₂O.
 - Add 0.38 µl 10% SDS.
 - Heat 95°C, 2 min.

- Slow cool at room temp. for 20 min.
Put on slide and hybridize overnight at 64°C.

Washing after the hybridization:

3X SSC/0.03% SDS: 2 min. 37.5 ml 20X SSC+0.75ml 10% SDS in 250ml H2O

1X SSC: 5 min. 12.5 ml 20X SSC in 250ml H2O

0.2X SSC: 5 min. 2.5 ml 20X SSC in 250ml H2O

Dry slides in centrifuge, 1000 RPM, 1min.

[273] Scan using appropriate Photomultiplier tube (PMT) and fluorescent excitation and emission channels.

[274] The results are shown in Table 1 and Table 2. The lists of genes come from colorectal tumors from a variety of stages of the disease. The genes that are up regulated in the tumors (overall) were also found to be expressed at a limited amount or not at all in the body map. The body map consists of at least 28 tissue types, including Adrenal Gland, Bladder, Bone Marrow, Brain, Breast, Cervix, Colon, Diaphragm, Heart, Kidney, Liver, Lung, Lymph Node, Muscle, Pancreas, Prostate, Rectum, Salivary Gland, Skin, Small Intestine, Spinal Cord, Spleen, Stomach, Testis, Thymus, Thyroid Trachea and Uterus. As indicated, some of the Accession numbers include expression sequence tags (ESTs). Thus, in one embodiment herein, genes within an expression profile, also termed expression profile genes, include ESTs and are not necessarily full length.

[275] Table 1 shows Accession numbers for 1747 genes upregulated in colon tumor tissue. The table provides the exemplar accession numbers, Unigene ID numbers, unique Eos codes, descriptions of the genes encoded, and relative amount of expression as compared with expression in other normal body tissue.

TABLE 1. GENES INVOLVED IN COLORECTAL CANCER

PKey	Primekey(unique probeset identifier)	Ex. Accn.	Exemplar accession number	Probeset	Eos Code number	Unigene#	Unigene number
Pkey	Probeset	Ex Accn	UniG ID	UniGene Title	Ratio Tum/Met/Body		
332264	EOS32195	N72849	Hs.115363	egfrregulin	17.8		
332718	EOS32947	L00058	Hs.79070	v-myc avian myelocytomatosis viral oncogene homolog	15.0		
312845	EOS12776	AI911215	Hs.186555	ESTs	14.3		
310257	EOS10188	AW389247	Hs.148826	ESTs	11.8		

	322567	EOS22468	AF151068		EST cluster (not in UniGene)	11.5
	331080	EOS30991	NF5081	Hs.21648	ESTs	10.3
	322303	EOS32234	W07149		EST cluster (not in UniGene)	9.8
5	301891	EOS01422	AF131855	Hs.106127	Homo sapiens clone 25056 mRNA sequence	9.5
	318524	EOS18456	AW291511	Hs.253687	ESTs	8.9
	314001	EOS13932	AW168495	Hs.253687	ESTs	7.8
	331183	EOS33114	T40798	Hs.8469	EST	7.3
	315429	EOS15361	AW001951	Hs.209882	ESTs	7.2
10	303344	EOS303275	AA256977	Hs.209466	ESTs; Highly similar to ubiquitin-conjugating enzyme [M.musculus]	6.7
	313825	EOS13556	AW468402	Hs.254020	ESTs	6.7
	307084	EOS07015	AI189027		EST singleton (not in UniGene) with exon hit	6.1
	314943	EOS14874	AW76797	Hs.184572	EST division cycle 2; G1 to S and G2 to M	6.1
	303753	EOS30364	AW595733	Hs.170015	ESTs	5.7
15	315593	EOS15524	AW198103	Hs.158154	ESTs	5.3
	313604	EOS13535	AA745325	Hs.182286	ESTs; Moderately similar to !!! ALU SUBFAMILY S2 WARNING ENTRY !!! [H.sapiens]	5.1
	321219	EOS12250	AA216696	Hs.180780	Homo sapiens agrin precursor mRNA; partial cds	5.1
	312814	EOS12545	AW76792	Hs.201154	ESTs	4.8
	323176	EOS23107	AW071648	Hs.123199	ESTs	4.8
20	317916	EOS17847	AS65071	Hs.159983	ESTs	4.7
	301846	EOS01777	R20002	Hs.6823	ESTs; Weakly similar to intrinsic factor-B12 receptor precursor [H.sapiens]	4.6
	311157	EOS11568	AW99102	Hs.196986	ESTs	4.6
	329840	EOS32571	AA417152	Hs.5101	protein regulator of cytokinesis 1	4.6
	311728	EOS11659	AW083000	Hs.184776	ribosomal protein L23a	4.5
	313774	EOS13705	AW136836	Hs.144583	ESTs	4.5
25	312339	EOS12320	AA504394		EST cluster (not in UniGene)	4.4
	315319	EOS15300	AA764918	Hs.256531	ESTs	4.3
	303756	EOS30367	AT738488	Hs.115938	ESTs	4.3
	301050	EOS00961	AW136873	Hs.144475	ESTs; Weakly similar to nitrogen inducible gene mig-2 [H.sapiens]	4.3
30	300319	EOS300250	AW157946	Hs.153506	ESTs; Weakly similar to microtubule-actin crosslinking factor [M.musculus]	4.3
	300694	EOS00695	AA444469	Hs.256809	ESTs	4.3
	300955	EOS00568	AA227892		EST cluster (not in UniGene) with exon hit	4.1
	315175	EOS15106	AA025842	Hs.162530	ESTs	4.1
35	330786	EOS30717	D60374	Hs.258712	EST	4.1
	310875	EOS12806	T47764	Hs.132917	EST	4.1
	313425	EOS13558	AA745689	Hs.186536	ESTs; Weakly similar to similar to zinc finger 5 protein from Gallus gallus; U51640 [H.sapiens]	4.0
	301804	EOS01735	AA581004		EST cluster (not in UniGene) with exon hit	4.0
40	332203	EOS32134	H49388	Hs.102082	EST	3.9
	322688	EOS22689	AA906228		EST cluster (not in UniGene)	3.8
	321624	EOS21456	N79126		EST cluster (not in UniGene)	3.8
	302476	EOS02407	AF142234		EST cluster (not in UniGene) with exon hit	3.8
	303326	EOS03226	AA205625	Hs.208067	ESTs	3.8
	310016	EOS09947	AW449612	Hs.152475	ESTs	3.7
	324871	EOS24802	AA269755	Hs.144932	ESTs	3.7
45	322842	EOS22818	AA905059	Hs.233456	ESTs; Weakly similar to KIAA0969 protein [H.sapiens]	3.7
	313171	EOS13102	N67879	Hs.157695	ESTs	3.7
	321638	EOS21659	AA366352	Hs.108932	ESTs	3.7
	320445	EOS20376	R33916		EST cluster (not in UniGene)	3.6
	302149	EOS03080	AA363794	Hs.152337	protein arginine N-methyltransferase 3(hnRNP methyltransferase S. cerevisiae)-like 3	3.6
50	316905	EOS16936	AW138241	Hs.210846	ESTs	3.6
	313166	EOS13097	AA801098	Hs.151500	ESTs	3.6
	322338	EOS23269	R74219	Hs.233348	S-phase kinase-associated protein 2 (p45)	3.5
	311434	EOS11365	AW016807	Hs.201582	ESTs	3.5
	312742	EOS12873	AA503633	Hs.116482	ESTs	3.4
55	323587	EOS23518	AA905927	Hs.141901	ESTs; Moderately similar to !!! ALU SUBFAMILY SP WARNING ENTRY !!! [H.sapiens]	3.4
	317390	EOS17321	AW136551	Hs.181246	ESTs	3.4
	318282	EOS15213	AA221865	Hs.144923	ESTs	3.4
	318515	EOS18498	AA40137	Hs.194989	ESTs	3.4
60	307586	EOS07517	AT285499		EST singleton (not in UniGene) with exon hit	3.4
	321052	EOS20983	AA372884	Hs.240770	nuclear cap binding protein subunit 2; 20kD	3.3
	324338	EOS24269	AL138357	Hs.247514	ESTs	3.3
	307517	EOS07448	AA273056	Hs.164689	ESTs	3.3
	314832	EOS14783	AA903735	Hs.137927	ESTs; Weakly similar to X-linked retinopathy protein [H.sapiens]	3.3
	324657	EOS24568	AA465142	Hs.255628	ESTs	3.2
65	314912	EOS14614	AA313345	Hs.167374	ESTs	3.2
	324790	EOS24721	AA334367	Hs.195337	ESTs	3.2
	315498	EOS15429	AA620639	Hs.116052	ESTs; Moderately similar to !!! ALU SUBFAMILY J WARNING ENTRY !!! [H.sapiens]	3.2
	312857	EOS12788	AA772279	Hs.126914	ESTs	3.2
	300762	EOS00693	AA497778	Hs.168053	ESTs	3.2
70	322557	EOS25518	c12_hs g1[682442]ref gn 6 + 126724 128667 ex 7 7 CDS1 2.44 244 3099		CH12_hs g1[682442]	3.2
	320654	EOS20585	AA263086	Hs.118112	ESTs	3.2
	318715	EOS16646	AA402268	Hs.170673	ESTs	3.1
	333279	EOS33210	CH22_522FG_126_1_LINK	EM:AC000550.GENSCAN.8-1	CH22_522FG_126_1_LINK	3.1
75	309689	EOS09620	AA226171	Hs.181357	laminin receptor 1 (67kD; ribosomal protein SA)	3.1
	323846	EOS23777	AA337621	Hs.137635	ESTs	3.1
	324678	EOS24609	AA907039	Hs.236511	ESTs; Moderately similar to RNA splicing-related protein [R.norvegicus]	3.1
	308392	EOS08293	AA151519		EST singleton (not in UniGene) with exon hit	3.1
	308615	EOS08648	AA795933		EST singleton (not in UniGene) with exon hit	3.0
80	315397	EOS15328	AA218940	Hs.137516	ESTs	3.0
	302238	EOS02167	AT128606	Hs.167558	zinc finger protein 161	3.0
	321893	EOS21624	AA700107	Hs.173737	ras-related G3 botulinum toxin substrate 1 (rho family; small GTP binding protein Rac1)	3.0
	330814	EOS30345	AA700107	Hs.247277	ESTs; Weakly similar to transcription-related protein [H.sapiens]	3.0
	302977	EOS20908	AA263124		EST cluster (not in UniGene)	3.0
85	327516	EOS27447	c_2_hs g1[17815]ref gn 6 + 190878 199216 ex 4 4 CDS1 9.15 139 1551		CH02_hs g1[17815]	2.9

333278	EOS33209	CH22_521FG_125_2_LINK	EM:AC005500.GENSCAN.7-2	2.9
332088	EOS02019	U77829	Hs.135630 achaele-scute complex (Drosophila) homolog-like 2	2.9
322718	EOS2649	AF150270	Hs.233322 ESTs; Weakly similar to cDNA EST EMBL:701156 comes from this gene [C.elegans]	2.9
329154	EOS29085	c_x_hs g 586868 ref	gn 2 - 200851 201356 ex 1 3 CDSi 30.28 506 1812	2.9
315978	EOS15609	AA830893	Hs.119789 CHX_hs g 586868	2.9
302677	EOS2608	Hs3227	Hs.132890 ESTs	2.9
315007	EOS14938	A1805883	Hs.125291 ESTs	2.9
303780	EOS03711	AA24014	Hs.243450 ESTs; Moderately similar to KIAA0456 protein [H.sapiens]	2.9
313682	EOS1293	AA417956	Hs.40782 ESTs	2.9
335915	EOS35746	CH22_3187FG_618_3_LINK	EM:AC005500.GENSCAN.510-3	2.8
32070	EOS32001	AA598545	Hs.228138 EST	2.8
315720	EOS15651	AW291875	Hs.163900 ESTs	2.8
311913	EOS11844	A136522	Hs.221417 ESTs	2.8
331014	EOS30945	H95597	Hs.30340 ESTs	2.8
322035	EOS21966	AL15717	EST cluster (not in UniGene)	2.8
338057	EOS37988	CH22_6558FG_4_LINK	EM:AC005500.GENSCAN.160-1	2.8
335829	EOS35760	CH22_3202FG_620_3_LINK	EM:AC005500.GENSCAN.160-1	2.8
312136	EOS12067	AW451468	Hs.209990 ESTs	2.8
303132	EOS00063	A829819	Hs.193330 ESTs	2.8
317548	EOS17479	A854187	Hs.195704 ESTs	2.8
325516	EOS25516	c12_hs g 58682462 ref	gn 1 + 73476 73574 ex 5 7 CDSi 8.52 99 309	2.7
334631	EOS34562	CH22_1938FG_416_7_LINK	EM:AC005500.GENSCAN.277-7	2.7
329156	EOS29087	c_x_hs g 586868 ref	gn 2 - 202013 202341 ex 2 3 CDSi 10.23 329 1814	2.7
318615	EOS18546	A1133817	Hs.191088 ESTs	2.7
300734	EOS00685	AW205197	Hs.240951 ESTs	2.7
324430	EOS24361	AA464018	EST cluster (not in UniGene)	2.7
322296	EOS22227	W76326	ESTs	2.7
303842	EOS03773	A1537304	Hs.251937 ESTs	2.7
320909	EOS20840	D62269	ESTs; Weakly similar to similar to PDZ domain [C.elegans]	2.7
325195	EOS25126	T20258	EST cluster (not in UniGene)	2.7
324959	EOS24890	AW367745	Hs.171443 ESTs; Weakly similar to actin binding protein MAYVEN [H.sapiens]	2.7
309967	EOS26628	A1291621	Hs.143137 ESTs	2.7
329367	EOS29296	c_x_hs g 58686842 ref	gn 1 - 87201 87587 ex 1 4 CDSi 8.13 387 3908	2.7
316897	EOS16628	AW293174	Hs.252627 ESTs	2.7
319600	EOS13531	AA429564	ESTs	2.7
301471	EOS01482	AA959514	Hs.123544 ESTs; Weakly similar to ORF YLL027w [S.cerevisiae]	2.6
300810	EOS00741	A1076890	Hs.186949 ESTs	2.6
319976	EOS19907	A48809	Hs.250824 ESTs	2.6
313434	EOS13365	W92070	Hs.231902 ESTs	2.6
333949	EOS33780	CH22_1118FG_290_8_LINK	EM:AC005500.GENSCAN.146-7	2.6
330744	EOS30675	AA406142	Hs.12393 dTDP-D-glucose 4,5-dehydratase	2.6
309098	EOS06329	AW081820	EST singleton (not in UniGene) with exon hit	2.6
338727	EOS36658	CH22_732FG_4_LINK	EM:AC005500.GENSCAN.500-2	2.6
324620	EOS24551	AA448021	EST cluster (not in UniGene)	2.6
335755	EOS35686	CH22_3122FG_604_4_LINK	EM:AC005500.GENSCAN.483-9	2.6
318568	EOS15789	AA797345	CH22_FGENES.604_4	2.6
307288	EOS07219	A105169	EST cluster (not in UniGene)	2.5
330542	EOS30473	U23942	EST singleton (not in UniGene) with exon hit	2.5
335896	EOS35827	CH22_3273FG_635_4_LINK	EM:AC005500.GENSCAN.525-6	2.5
316578	EOS15509	AA775623	Hs.211683 CH22_FGENES.635_4	2.5
329193	EOS29124	c_x_hs g 5868716 ref	gn 3 + 168095 168181 ex 9 9 CDSi -1.11 87 2064	2.5
315193	EOS15124	A1241331	Hs.131765 CHX_hs g 5868716	2.5
319478	EOS19409	R06841	ESTs	2.5
334727	EOS34598	CH22_2038FG_424_1_LINK	EM:AC005500.GENSCAN.285-3	2.5
328113	EOS28044	c_6_hs g 5868024 ref	gn 2 - 80378 80491 ex 3 3 CDSi 3.99 114 3247	2.5
315214	EOS15145	A1915927	Hs.34771 CHX_hs g 5868024	2.5
324718	EOS24648	A1557019	Hs.115467 ESTs	2.5
313326	EOS13257	A1068120	Hs.122329 ESTs	2.5
319480	EOS19411	R06933	Hs.184221 ESTs	2.5
317902	EOS17833	A1828602	Hs.211265 ESTs	2.5
323341	EOS23872	AL119475	Hs.192389 ESTs	2.5
330003	EOS36934	CH22_3385FG_664_4_LINK	DJ3210.GENSCAN.5-4	2.5
322992	EOS22923	AA142691	Hs.193165 CH22_FGENES.664_4	2.5
314811	EOS14842	AW292329	Hs.163491 ESTs	2.5
313903	EOS13534	AW466119	EST cluster (not in UniGene)	2.5
308469	EOS06400	AA983792	EST singleton (not in UniGene) with exon hit	2.5
324715	EOS24646	A1739108	EST cluster (not in UniGene)	2.5
302455	EOS02386	AA356923	Hs.240770 nuclear cap binding protein subunit 2; 20KD	2.4
321023	EOS29954	H25135	Hs.125608 ESTs	2.4

	302099	EOS020200	AI021397	Hs.137576	ribosomal protein L34 pseudogene 1	2.4
	314092	EOS14023	AI084040	Hs.228946	ESTs	2.4
	316587	EOS18518	AA779704	Hs.168830	ESTs	2.4
5	303702	EOS030633	AW500748	Hs.22461	ESTs; Weakly similar to 73 kDa subunit of cleavage and polyadenylation specificity factor [H.sapiens]	2.4
	301822	EOS01753	X17033	Hs.1142	integrin, alpha 2 (CD49b; alpha 2 subunit of VLA-2 receptor)	2.4
	322644	EOS25825	AI020872	Hs.152461	EST cluster (not in UniGene)	2.4
	323333	EOS23264	AA228883	Hs.152461	EST cluster (not in UniGene)	2.4
	301954	EOS01885	AI009936	Hs.118138	nuclear receptor subfamily 1; group 1; member 2	2.4
	331363	EOS13294	AA421562	Hs.91011	anterior gradient 2 (Xenopus laevis) homolog	2.4
10	303811	EOS03742	AW182340	Hs.244155	ESTs; Weakly similar to DNA TOPOISOMERASE I [H.sapiens]	2.4
	302423	EOS08174	AI650037	Hs.152461	EST singleton (not in UniGene) with exon hit	2.4
	338021	EOS33652	CH22_3404FG_669_10_LINK	CH22_3404FG_669_10_LINK.CH22_3404FG_669_10.CH22_FGENES.669_10	CH22_FGENES.669_10	2.4
15	334789	EOS34720	CH22_2101FG_432_14_LINK	CH22_2101FG_432_14_LINK.CH22_2101FG_432_14.CH22_FGENES.432_14	CH22_FGENES.432_14	2.4
	320807	EOS20738	AA096110	Hs.189536	Homio sapiens clone 24838 mRNA sequence	2.4
	328093	EOS28834	c_8_hs_gli5686514[ref] on 1	+ 23825 24498 ex 3 5 CDS: 91.18 844 219	CH.08_hs_gli5686514	2.4
20	338756	EOS36860	CH22_7581FG_LINK	CH22_7581FG_LINK.CH22_7581FG_LINK.CH22_FGENES.517-6	CH22_FGENES.517-6	2.4
	333769	EOS03700	CH22_1039FG_271_8_LINK	CH22_1039FG_271_8_LINK.CH22_1039FG_271_8.CH22_FGENES.271_8	CH22_FGENES.271_8	2.3
25	303597	EOS030528	AI792141	Hs.143560	ESTs; Weakly similar to brain mitochondrial carrier protein-1 [H.sapiens]	2.3
	305869	EOS05829	AA872838	Hs.242463	keratin 8	2.3
	304439	EOS04370	AA398882	Hs.152461	EST singleton (not in UniGene) with exon hit	2.3
	301604	EOS01535	AA373124	Hs.105837	ESTs; Weakly similar to C17G10.1 [C.elegans]	2.3
	315071	EOS15002	AA552090	Hs.152461	ESTs	2.3
	303665	EOS030466	U15096	Hs.1545	caudal type homeo box transcription factor 1	2.3
30	331599	EOS13520	AI71087	Hs.141856	ESTs	2.3
	303216	EOS03147	AA581439	Hs.152328	ESTs	2.3
	324988	EOS24919	T06997	Hs.152328	EST cluster (not in UniGene)	2.3
	312998	EOS12927	AA249018	Hs.152328	EST cluster (not in UniGene)	2.3
	302314	EOS32245	T25862	Hs.101774	ESTs	2.3
35	313325	EOS13256	AA206111	Hs.127632	ESTs	2.3
	322591	EOS22522	C18965	Hs.159473	ESTs	2.3
	335496	EOS35427	CH22_2848FG_571_4_LINK	CH22_2848FG_571_4_LINK.CH22_2848FG_571_4_LINK.CH22_FGENES.571_4	CH22_FGENES.571_4	2.3
40	315135	EOS15086	AA627561	Hs.192446	ESTs	2.3
	319458	EOS19419	AW203040	Hs.152328	EST cluster (not in UniGene)	2.3
	323571	EOS23502	AA584133	Hs.153260	C-99-interacting protein	2.3
	322826	EOS22757	AI007883	Hs.156932	ESTs	2.3
	322221	EOS22152	AI890619	Hs.179662	nucleosome assembly protein 1-like 1	2.3
	312442	EOS12173	AI300207	Hs.125276	ESTs	2.3
45	315238	EOS15158	AA583867	Hs.170990	ESTs	2.3
	315158	EOS15099	AA822130	Hs.152524	ESTs	2.3
	300504	EOS00435	AW204824	Hs.192927	ESTs; Weakly similar to Lim kinase [H.sapiens]	2.3
	323243	EOS23174	W44372	Hs.152328	EST cluster (not in UniGene)	2.3
50	331528	EOS13559	R00965	Hs.204079	ESTs	2.3
	302748	EOS20677	AA128302	Hs.152328	EST cluster (not in UniGene)	2.3
	324596	EOS24529	AA502559	Hs.163966	ESTs	2.3
	308667	EOS06898	AI758754	Hs.152328	EST singleton (not in UniGene) with exon hit	2.2
	302944	EOS02875	AA340708	Hs.256204	ESTs; Weakly similar to cyclic nucleotide-gated channel beta subunit [R.norvegicus]	2.2
	316291	EOS16222	AW373274	Hs.150704	ESTs	2.2
55	315296	EOS15227	AA878905	Hs.152328	ESTs	2.2
	334150	EOS34081	CH22_1426FG_339_1_LINK	CH22_1426FG_339_1_LINK.CH22_1426FG_339_1_LINK.CH22_FGENES.339_1	CH22_FGENES.339_1	2.2
60	331380	EOS13111	AA453268	Hs.246131	ESTs	2.2
	321795	EOS21726	AI706896	Hs.222446	ESTs	2.2
	331493	EOS31424	N34357	Hs.44571	ESTs	2.2
	312990	EOS12821	AI813654	Hs.127478	ESTs	2.2
	315583	EOS15514	AW005622	Hs.126555	ESTs	2.2
	314306	EOS14237	AI887901	Hs.192425	ESTs	2.2
	314138	EOS14069	AA740616	Hs.152328	EST cluster (not in UniGene)	2.2
65	302656	EOS02587	AW203005	Hs.220905	ESTs	2.2
	313564	EOS13495	AA810141	Hs.192182	ESTs	2.2
	332792	EOS32723	CH22_8FG_3_2_LINK	CH22_8FG_3_2_LINK.CH22_8FG_3_2_LINK.CH22_FGENES.3-2	CH22_FGENES.3-2	2.2
70	332020	EOS11951	AA488895	Hs.105219	ESTs	2.2
	315143	EOS15074	AA878334	Hs.192734	ESTs	2.2
	313385	EOS13316	AA520367	Hs.176711	ESTs	2.2
	323835	EOS28786	AL042005	Hs.152328	EST cluster (not in UniGene)	2.2
	314014	EOS13945	AW291847	Hs.121715	ESTs; Weakly similar to HP protein [H.sapiens]	2.2
	336016	EOS35947	CH22_3399FG_669_5_LINK	CH22_3399FG_669_5_LINK.CH22_3399FG_669_5_LINK.CH22_FGENES.669_5	CH22_FGENES.669_5	2.2
75	323218	EOS23149	AF131848	Hs.13396	Homio sapiens clone 25026 mRNA sequence	2.2
	338059	EOS37990	CH22_8561FG_LINK	CH22_8561FG_LINK.CH22_8561FG_LINK.CH22_FGENES.160-4	CH22_FGENES.160-4	2.2
	302613	EOS02544	AA371059	Hs.251636	ubiquitin specific protease 3	2.2
80	304852	EOS04783	AA589595	Hs.152328	EST singleton (not in UniGene) with exon hit	2.2
	305457	EOS03385	AI059859	Hs.152328	EST singleton (not in UniGene) with exon hit	2.2
	311736	EOS11667	AA765897	Hs.152328	EST cluster (not in UniGene)	2.2
	334183	EOS34114	CH22_1464FG_350_13_LINK	CH22_1464FG_350_13_LINK.CH22_1464FG_350_13_LINK.CH22_FGENES.350_13	CH22_FGENES.350_13	2.2
85	315021	EOS14952	AA533447	Hs.152328	EST cluster (not in UniGene)	2.2
	303013	EOS02944	F07898	Hs.214190	interleukin enhancer binding factor 1	2.2
	315006	EOS14937	AI538613	Hs.135657	ESTs	2.2

5	337534	EOS37465	CH22_5803FG_828_3	CH22_FGENES.828-3	2,2	
	303276	EOS30207	AA431599	Ha.132799	ESTs	2,1
	319617	EOS19548	AW247252	Ha.75514	nucleoside phosphorylase	2,1
	330760	EOS30691	AA448663	Ha.30469	ESTs	2,1
	319645	EOS19476	R83716	Ha.14355	ESTs	2,1
10	312252	EOS12163	AI126388	Ha.14365	ESTs	2,1
	322882	EOS22813	AW248508	Ha.2491	DGeorge syndrome critical region gene 2	2,1
	312684	EOS12815	AW284020	Ha.117721	ESTs	2,1
	315782	EOS15713	AW515455	Ha.115558	ESTs; Weakly similar to !!! ALU SUBFAMILY J WARNING ENTRY !!! [H.sapiens]	2,1
	320076	EOS20007	AI653733	Ha.204079	ESTs	2,1
15	303566	EOS00497	H86709	Ha.21371	son of sevenless (Drosophila) homolog 1	2,1
	300908	EOS00838	AA618335	Ha.146137	ESTs; Weakly similar to putative [C.elegans]	2,1
	314778	EOS14709	AW079559	Ha.152258	ESTs	2,1
	319233	EOS19164	R21054	Ha.211922	ESTs	2,1
	335488	EOS35419	CH22_2840FG_570_20_LINK	EM.AC005500.GENSCAN.460-15	CH22_FGENES.570_20	2,1
20	334616	EOS34547	CH22_1923FG_411_15_LINK	EM.AC005500.GENSCAN.274-22	CH22_FGENES.411_15	2,1
	306792	EOS06723	AI042426	EST singleton (not in UniGene) with exon hit	2,1	
	301861	EOS01592	AI815558	EST cluster (not in UniGene) with exon hit	2,1	
	311532	EOS11263	AW292247	Ha.255052	ESTs	2,1
	314785	EOS14716	AI583226	Ha.135184	ESTs	2,1
25	301490	EOS01391	AW196758	Ha.165998	DKFZP564M2423 protein	2,1
	332015	EOS13146	AA487910	Ha.202800	ESTs; Weakly similar to !!! ALU CLASS B WARNING ENTRY !!! [H.sapiens]	2,1
	321929	EOS21480	AD28506	Ha.145066	ESTs	2,1
	323740	EOS23671	AA324643	Ha.246106	ESTs	2,1
	338019	EOS35950	CH22_3402FG_669_8_LINK	CH22_DJ3210.GENSCAN.9-13	CH22_FGENES.669_8	2,1
30	314954	EOS14885	AA521381	Ha.187726	ESTs	2,1
	303037	EOS02968	AF115395	EST cluster (not in UniGene) with exon hit	2,1	
	302056	EOS01987	AA575332	Ha.126082	ESTs; Moderately similar to ROSA26AS [M.musculus]	2,1
	315178	EOS15109	AW362945	Ha.162459	ESTs	2,1
	332246	EOS32177	N57927	Ha.120777	ESTs; Weakly similar to RNA POLYMERASE II ELONGATION FACTOR ELL2 [H.sapiens]	2,1
35	334288	EOS34219	CH22_1577FG_369_18_LINK	EM.AC005500.GENSCAN.229-18	CH22_FGENES.369_18	2,1
	324690	EOS24621	N88286	Ha.132808	ESTs; Weakly similar to Similar to S.pombe -rtd4/cut5+product [H.sapiens]	2,1
	302527	EOS05188	AA679005	Ha.13601	EST singleton (not in UniGene) with exon hit	2,1
	311315	EOS11246	AW450536	Ha.209260	ESTs	2,1
	311988	EOS11919	AW016096	Ha.13601	ESTs	2,1
40	302538	EOS02599	AA463798	Ha.102699	ESTs; Weakly similar to C11D2.4 [C.elegans]	2,1
	302551	EOS20462	W03891	Ha.24584	ESTs; Moderately similar to RNA polymerase I associated factor [M.musculus]	2,1
	323004	EOS23335	AI751438	Ha.182827	ESTs; Weakly similar to !!! ALU SUBFAMILY S WARNING ENTRY !!! [H.sapiens]	2,1
	308552	EOS06763	AI829548	Ha.182937	peptidylprolyl isomerase A (cyclophilin A)	2,1
	302621	EOS20432	N51464	Ha.24743	ESTs	2,1
45	331306	EOS13237	AA252079	Ha.53951	disulfund (Drosophila) homolog	2,1
	314941	EOS14572	AA515902	Ha.130650	ESTs	2,1
	336884	EOS36815	CH22_4167FG_46_1	CH22_FGENES.46-1	2,1	
	301137	EOS01068	AF049588	Ha.137096	ESTs	2,1
	339454	EOS36365	CH22_7128FG_LINK	EM.AC005500.GENSCAN.390-4	CH22_FGENES.390-4	2,1
50	309700	EOS09631	AW241170	Ha.179661	Homo sapiens clone 24703 beta-tubulin mRNA; complete cds	2,1
	330262	EOS30193	c_5_p2_gi[6671884]gbA gn	1 + 67913 68053 ex 3 3 CDSI 5.41 141 597	CH.05_p2 gi[6671884]	2,1
	324163	EOS24094	AA048827	Ha.134651	ESTs	2,1
	316493	EOS16424	AA766142	Ha.131810	ESTs; Weakly similar to !!! ALU SUBFAMILY J WARNING ENTRY !!! [H.sapiens]	2,1
	311873	EOS11804	AA730045	Ha.187686	ESTs	2,1
55	328757	EOS26688	c20_hs gi[6248610]ref gn 3	+ 74531 74597 ex 1 3 CDSI 9.52 67 1416	CH.20_hs gi[6248610]	2,1
	319167	EOS19088	F05894	Ha.250138	protein phosphatase 2C; magnesium-dependent; catalytic subunit	2,1
	318011	EOS15942	AW516953	Ha.201372	ESTs	2,1
	313635	EOS13566	AA507227	Ha.6390	ESTs	2,1
	310227	EOS09558	AW448009	Ha.126457	ESTs	2,1
60	339692	EOS36993	CH22_4198FG_41_1	CH22_FGENES.41-1	2,1	
	334648	EOS34579	CH22_1958FG_417_15_LINK	EM.AC005500.GENSCAN.278-15	CH22_FGENES.417_15	2,1
	308676	EOS08607	AI761036	EST singleton (not in UniGene) with exon hit	2,1	
	312047	EOS11976	AA582275	Ha.14259	ESTs	2,1
	324626	EOS24757	AA704806	Ha.145842	ESTs	2,1
65	322889	EOS22820	AA081924	Ha.211417	ESTs	2,1
	316345	EOS16276	AW139408	Ha.152940	ESTs	2,1
	313922	EOS13853	AI702538	Ha.100057	ESTs	2,1
	319423	EOS13854	T83024	Ha.15119	ESTs	2,1
	320244	EOS20175	AA299922	Ha.129778	gasronintestinal peptide	2,1
70	308957	EOS08888	AI89642	EST singleton (not in UniGene) with exon hit	2,1	
	334223	EOS34154	CH22_1507FG_360_4_LINK	EM.AC005500.GENSCAN.218-4	CH22_FGENES.360_4	2,1
	302880	EOS02911	W93435	EST cluster (not in UniGene) with exon hit	1,9	
	312153	EOS12064	AA792950	Ha.153028	EST singleton (not in UniGene) with exon hit	1,9
	329460	EOS26391	c19_hs gi[5867400]ref gn 3	- 124633 124935 ex 1 2 CDSI 18.03 300 1731	CH.19_hs gi[5867400]	1,9
75	319942	EOS19893	H06350	Ha.135056	ESTs	1,9
	307064	EOS06995	AI149335	EST singleton (not in UniGene) with exon hit	1,9	
	331608	EOS15359	N89861	Ha.44162	ESTs; Weakly similar to cDNA EST yk342h12.5 comes from this gene [C.elegans]	1,9
	328142	EOS28073	c_6_hs gi[5868050]ref gn 1	- 9696 9778 ex 2 6 CDSI 11.11 123 3339	CH.06_hs gi[5868050]	1,9
	312527	EOS12458	AI895622	Ha.191271	ESTs	1,9

	318581	EOS18512	AA769058	EST cluster (not in UniGene)	1.9
	318978	EOS19910	AB018261	Ha.107479 KIA0238 gene product	1.9
	336107	EOS36036	CH22_3496FG_666_3_LINK	EM:AC005500.GENSCAN.4-3	1.9
				CH22_FGENES.696_3	1.9
5	305232	EOS05163	AA670052	Ha.195188 glyceraldehyde-3-phosphate dehydrogenase	1.9
	315043	EOS14974	AA060538	Ha.130732 ESTs	1.9
	325377	EOS23936	AA133390	Ha.8454 protein kinase; cAMP-dependent; regulatory; type II; alpha	1.9
	338250	EOS38191	CH22_6963FG_LINK	EM:AC005500.GENSCAN.279-10	1.9
				CH22_EM:AC005500.GENSCAN.279-10	1.9
10	334891	EOS34822	CH22_2208FG_462_5_LINK	EM:AC005500.GENSCAN.341-8	1.9
				CH22_FGENES.462_5	1.9
	316055	EOS15986	AA603880	EST cluster (not in UniGene)	1.9
	312414	EOS12345	A915014	Ha.164235 ESTs; Weakly similar to !!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.9
	300225	EOS00156	A989993	Ha.197505 ESTs	1.9
15	332607	EOS32538	R41791	Ha.36566 LIM domain kinase 1	1.9
	312405	EOS12336	A523675	EST cluster (not in UniGene)	1.9
	315626	EOS13936	A761756	Ha.204674 ESTs	1.9
	337755	EOS37696	CH22_6105FG_LINK	EM:AC000097.GENSCAN.109-2	1.9
				CH22_EM:AC000097.GENSCAN.109-2	1.9
20	323216	EOS23147	AA332145	EST cluster (not in UniGene)	1.9
	334672	EOS34803	CH22_2188FG_450_2_LINK	EM:AC005500.GENSCAN.339-2	1.9
				CH22_FGENES.450_2	1.9
	332034	EOS31965	AA489447	Ha.112019 ESTs; Moderately similar to !!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.9
	332103	EOS32034	AA609161	Ha.112657 ESTs; Weakly similar to ORF YOR243; [S.cerevisiae]	1.9
25	318196	EOS18127	AO56776	Ha.133397 ESTs	1.9
	329141	EOS29072	c_x_ha_gi601706[g] [n]	1 + 343824 343997 ex 2 3 CDSi 8.53 74 1715	1.9
				CH.X_ha_gi6017060	1.9
	321539	EOS21470	N9819	Ha.62461 ARP2 (actin-related protein 2; yeast) homolog	1.9
	313881	EOS13812	AA535530	Ha.16331 ESTs	1.9
	314046	EOS13977	AW021917	Ha.161678 ESTs	1.9
	336045	EOS35976	CH22_3430FG_679_7_LINK	EM:AC005500.GENSCAN.18-8	1.9
				CH22_FGENES.679_7	1.9
30	324799	EOS24730	AW272262	Ha.250468 ESTs	1.9
	312556	EOS12587	AW152449	Ha.225469 ESTs	1.9
	324662	EOS24563	AW504689	EST cluster (not in UniGene)	1.9
35	323930	EOS23861	AA570686	Ha.193203 ESTs	1.9
	314465	EOS14396	AA602917	Ha.156974 ESTs	1.9
	335897	EOS35028	CH22_3274FG_635_5_LINK	EM:AC005500.GENSCAN.525-7	1.9
				CH22_FGENES.635_5	1.9
40	321748	EOS21677	AB065500	Ha.102852 ESTs; Weakly similar to KIA0437 [H.sapiens]	1.9
	335687	EOS35618	CH22_3048FG_596_2_LINK	EM:AC005500.GENSCAN.488-2	1.9
				CH22_FGENES.596_2	1.9
	330731	EOS30662	AA278816	Ha.177204 ESTs	1.9
	316547	EOS16473	AO79476	Ha.109557 ESTs; Highly similar to CGI-89 protein [H.sapiens]	1.9
45	336373	EOS36510	CH22_3791FG_821_7_LINK	EM:AC005500.GENSCAN.4-19	1.9
				CH22_FGENES.821_7	1.9
	305691	EOS05622	AA813590	Ha.119500 karyopherin alpha 4 (importin alpha 3)	1.9
	310639	EOS10570	AW289082	Ha.175162 ESTs	1.9
50	327481	EOS27412	c_2_ha_gi586778[g] [n]	3 + 104472 104679 ex 1 4 CDSi 14.33 202 1308	1.9
				CH.02_ha_gi5867783	1.9
	301910	EOS01841	T84852	Ha.98370 cytochrome P540 family member predicted from ESTs	1.9
	335478	EOS36409	CH22_2830FG_569_1_LINK	EM:AC005500.GENSCAN.456-1	1.9
				CH22_FGENES.569_1	1.9
55	331135	EOS31096	R61398	Ha.4197 ESTs	1.9
	335690	EOS35621	CH22_3051FG_596_5_LINK	EM:AC005500.GENSCAN.488-5	1.9
				CH22_FGENES.596_5	1.9
	308047	EOS07978	AI459833	EST singleton (not in UniGene) with exon hit	1.9
	334500	EOS34431	CH22_1800FG_367_16_LINK	EM:AC005500.GENSCAN.269-18	1.9
				CH22_FGENES.367_16	1.9
60	338250	EOS38181	CH22_6848FG_LINK	EM:AC005500.GENSCAN.269-2	1.9
				CH22_EM:AC005500.GENSCAN.269-2	1.9
	320618	EOS20549	AI220278	Ha.235528 EST	1.8
	335044	EOS34975	CH22_2367FG_480_1_LINK	EM:AC005500.GENSCAN.374-1	1.9
				CH22_FGENES.480_1	1.8
65	313789	EOS13720	AI167810	Ha.217743 ESTs	1.9
	319111	EOS11842	AO871223	Ha.114344 ESTs; Weakly similar to !!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.8
	320180	EOS20111	AA046203	Ha.193974 ESTs; Weakly similar to alternatively spliced product using exon 13A [H.sapiens]	1.8
	311036	EOS10967	AE53227	Ha.214039 ESTs	1.8
70	323903	EOS23834	AA773580	Ha.193598 ESTs	1.8
	318676	EOS18007	T57448	Ha.15467 ESTs; Moderately similar to putative phosphoinositide 5-phosphatase type II [M.musculus]	1.8
	303007	EOS02938	AA478876	Ha.7037 pallid (mouse) homodog; pallidin	1.8
	334698	EOS34737	CH22_2119FG_435_7_LINK	EM:AC005500.GENSCAN.296-6	1.8
				CH22_FGENES.435_7	1.8
75	311767	EOS11698	AI076886	Ha.190066 ESTs	1.8
	331750	EOS31881	AA284372	Ha.111471 ESTs	1.8
	314672	EOS14003	AI141254	Ha.239726 ESTs	1.8
	314071	EOS14002	AA192455	Ha.189640 ESTs	1.8
	328450	EOS28361	c_7_ha_gi5868425[g] [n]	2 + 209192 209321 ex 2 3 CDSi 10.41 130 1407	1.8
				CH.07_ha_gi5868425	1.8
80	328657	EOS28788	c_7_ha_gi581927[g] [n]	3 - 80657 81051 ex 1 1 CDSi 41.51 495 6090	1.8
				CH.07_ha_gi581927	1.8
	313781	EOS13712	AA078836	EST cluster (not in UniGene)	1.8
	336953	EOS36884	CH22_4746FG_361_22_LINK	EM:AC005500.GENSCAN.361-22	1.8
	300233	EOS00164	AI380777	Ha.189402 ESTs	1.8
85	328662	EOS26793	c20_ha_gi5952465[g] [n]	2 + 107702 107782 ex 12 13 CDSi 3.62 81 2149	1.8
				CH.20_ha_gi5952465	1.8

5	312954	EOS12295	R40111	Hs.187618	ESTs	1.8	
	321541	EOS21472	A022092	Hs.254467	ESTs	1.8	
	307432	EOS07363	A024259	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.8	
	320821	EOS20852	R94038	Hs.199538	inhibin; beta C	1.8	
	333110	EOS33041	CH22_338FG_79_16_LINK	EM-AC000097.GENSCAN.59-15	CH22_FGENES.79_16	1.8	
10	324914	EOS24845	A4847510	Hs.161292	ESTs	1.8	
	312681	EOS12612	A028149	Hs.193124	pyruvate dehydrogenase kinase; isoenzyme 3	1.8	
	335697	EOS36628	CH22_3058FG_596_12_LINK	EM-AC005500.GENSCAN.488-13	CH22_FGENES.596_12	1.8	
	303462	EOS08363	A671311	Hs.104613	EST singleton (not in UniGene) with exon hit	1.8	
	312138	EOS12069	T89405	Hs.218851	ESTs; Weakly similar to III ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.8	
15	309116	EOS09047	A927149	Hs.29797	ribosomal protein L10	1.8	
	307301	EOS20661	AA534539	Hs.151072	ESTs	1.8	
	300844	EOS00775	AL042759	Hs.191762	ESTs	1.8	
	335750	EOS37501	CH22_565FG_LINK_C65E1	GENSCAN.4-2	CH22_C65E1.GENSCAN.4-2	1.8	
	332756	EOS32687	D63479	Hs.115907	diacylglycerol kinase; delta (130kD)	1.8	
20	332161	EOS32092	AA621523	Hs.105444	ESTs	1.8	
	300942	EOS00873	AW275006	Hs.195989	ESTs	1.8	
	300380	EOS00311	AW468056	Hs.257712	ESTs; Weakly similar to KIAA0986 protein [H.sapiens]	1.8	
	328763	EOS26714	c_7_hs	gl 5868309 ref	gn 5 - 73658 73822 ex 2 CDS1 0.78 165 5371	CH_07_hs gl 5868309	1.8
	307542	EOS07473	A028059		EST singleton (not in UniGene) with exon hit	1.8	
25	331975	EOS31906	AA464972	Hs.199624	ESTs	1.8	
	321532	EOS21463	T77886	Hs.83428	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (p105)	1.8	
	318221	EOS18652	Z28504		EST cluster (not in UniGene)	1.8	
	302124	EOS02055	A0203967	Hs.145078	regulator of differentiation (in S. pombe) 1	1.8	
	323541	EOS23472	A185116	Hs.104613	ESTs; Weakly similar to Similar to S.cerevisiae hypothetical protein L3111 [H.sapiens]	1.8	
30	331057	EOS330858	N71369	Hs.28143	ESTs	1.8	
	316660	EOS16791	AW130099	Hs.127489	ESTs	1.8	
	330601	EOS30632	U09016	Hs.82845	Human clone 23815 mRNA sequence	1.8	
	307334	EOS07265	A121481	Hs.220615	ESTs; Weakly similar to TFIIH protein [H.sapiens]	1.8	
	323195	EOS23126	AA049382	Hs.117950	multifunctional polypeptide similar to SAICAR synthetase and AIR carboxylase	1.8	
35	300358	EOS02787	AA095699	Hs.944	glucose phosphate isomerase	1.8	
	321553	EOS21484	H82449	Hs.116406	ESTs	1.8	
	332705	EOS32636	T59161	Hs.75293	thymosin; beta 10	1.8	
	333139	EOS33070	CH22_368FG_83_16_LINK	EM-AC000097.GENSCAN.67-19	CH22_FGENES.83_16	1.8	
	338997	EOS36928	CH22_7881FG_LINK_DAS9H18	GENSCAN.8-22	CH22_DAS9H18.GENSCAN.8-22	1.8	
40	301509	EOS01440	A025435	Hs.117532	ESTs	1.8	
	314822	EOS14453	A723231	Hs.187750	ESTs; Moderately similar to III ALU CLASS C WARNING ENTRY !!!! [H.sapiens]	1.8	
	303072	EOS33063	AF187893		EST cluster (not in UniGene) with exon hit	1.8	
	305271	EOS05202	AA678955		EST singleton (not in UniGene) with exon hit	1.8	
	335287	EOS36218	CH22_2629FG_526_11_LINK	EM-AC005500.GENSCAN.420-4	CH22_FGENES.526_11	1.8	
45	321296	EOS21217	A038040		EST cluster (not in UniGene)	1.8	
	318740	EOS18671	NM_002543		EST cluster (not in UniGene)	1.8	
	323465	EOS23396	AA287406		EST cluster (not in UniGene)	1.8	
	300611	EOS00542	N75450		EST cluster (not in UniGene) with exon hit	1.8	
	306235	EOS06166	AA932299		EST singleton (not in UniGene) with exon hit	1.8	
50	333671	EOS36652	CH22_4244FG_83_17_LINK	EM-AC005500.GENSCAN.83-17	CH22_FGENES.83-17	1.8	
	311291	EOS11222	A726201	Hs.122684	ESTs	1.8	
	310247	EOS10178	A224982	Hs.211454	ESTs	1.8	
	316584	EOS16495	A143571	Hs.168799	ESTs; Weakly similar to III ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	1.8	
	328170	EOS28101	c_8_hs	gl 586807 ref	gn 1 + 83170 53295 ex 9 CDS1 13.31 126 3591	CH_08_hs gl 586807	1.8
55	300909	EOS00840	AW265479	Hs.154903	ESTs; Weakly similar to Abi substrate ena [D.melanogaster]	1.8	
	330869	EOS30800	AA115197	Hs.183702	ESTs	1.8	
	311048	EOS10679	AA506952	Hs.210506	ESTs	1.8	
	333764	EOS33695	CH22_1031FG_271_3_LINK	EM-AC005500.GENSCAN.127-3	CH22_FGENES.271_3	1.8	
	338862	EOS36793	CH22_7715FG_LINK_DJ3210	GENSCAN.1-6	CH22_DJ3210.GENSCAN.1-6	1.8	
60	331467	EOS31398	N22206	Hs.43112	ESTs	1.8	
	327742	EOS27673	c_5_hs	gl 5867944 ref	gn 3 - 143307 143512 ex 1 3 CDS1 11.07 206 172	CH_05_hs gl 5867944	1.8
	320955	EOS20886	AL049415	Hs.204290	Homo sapiens mRNA; cDNA DKFZ588N2119 (from clone DKFZ556N2119)	1.8	
	323589	EOS23520	AW360054	Hs.192843	ESTs	1.8	
	319951	EOS16862	AA307965	Hs.14559	ESTs	1.8	
65	335763	EOS33654	CH22_1030FG_271_2_LINK	EM-AC005500.GENSCAN.127-2	CH22_FGENES.271_2	1.8	
	331046	EOS30977	N65563	Hs.191358	ESTs	1.7	
	320001	EOS18932	AA873350		EST cluster (not in UniGene)	1.7	
	318689	EOS16800	A054980	Hs.134604	ESTs	1.7	
	310774	EOS10705	AW134483	Hs.164371	ESTs	1.7	
70	319379	EOS19310	T91443	Hs.193963	ESTs	1.7	
	321549	EOS21480	AA470984	Hs.161947	ESTs	1.7	
	300823	EOS00754	A186308	Hs.222655	ESTs; Weakly similar to putative zinc finger protein NY-REN-34 antigen [H.sapiens]	1.7	
	324228	EOS24159	A7818146	Hs.207780	ESTs	1.7	
	313902	EOS13633	A1308165	Hs.156242	ESTs	1.7	
75	308928	EOS08859	A186308		EST singleton (not in UniGene) with exon hit	1.7	
	333770	EOS33701	CH22_1037FG_272_1_LINK	EM-AC005500.GENSCAN.127-1	CH22_FGENES.272_1	1.7	
	316834	EOS16865	A1571647	Hs.146170	ESTs	1.7	

	313218	EOS13150	N74924	Hs.182099	ESTs	1.7
	317360	EOS17291	A1125252	Hs.126419	ESTs	1.7
	303530	EOS0461	A274451	Hs.259744	ESTs	1.7
5	334739	EOS34670	CH22_2051FG_424_14_LINK	EM:AC005500.GENSCAN.285-18	CH22_FGENES.424_14	1.7
	337670	EOS37801	CH22_5896FG_LINK	EM:AC000097.GENSCAN.57-2	CH22_FGENES.589_2	1.7
	312079	EOS12010	T79745	Hs.189717	ESTs	1.7
	320211	EOS20142	AL038402	Hs.125783	DEME-6 protein	1.7
10	316218	EOS16149	AW207642	Hs.174021	ESTs	1.7
	335682	EOS35613	CH22_3043FG_565_2_LINK	EM:AC005500.GENSCAN.487-11	CH22_FGENES.565_2	1.7
	330696	EOS30627	AA022632	Hs.15825	ESTs	1.7
	314449	EOS14380	AL042667	Hs.225539	ESTs	1.7
15	317192	EOS11903	N51511	Hs.188449	ESTs	1.7
	307971	EOS07622	AS18285	Hs.162371	prothymosin, alpha (gene sequence 28)	1.7
	336249	EOS36180	CH22_6847FG_LINK	EM:AC005500.GENSCAN.269-1	CH22_FGENES.684_7	1.7
20	326399	EOS26330	c19_hs	g15867353[ref] gn 1 + 6385 5536 ex 6 6 CDS1 10.69 152 684	CH_19_hs	1.7
	313290	EOS13621	A1753247	Hs.206454	ESTs	1.7
	301615	EOS01548	W39477	Hs.206454	ESTs	1.7
	307034	EOS08965	A1142526	Hs.155029	EST cluster (not in UniGene) with exon hit	1.7
	313577	EOS13508	AA565051	Hs.155029	ESTs	1.7
25	324703	EOS24834	AA060282	Hs.31085	Homo sapiens mRNA for cytochrome b5, partial cds	1.7
	321317	EOS21248	AB210600	Hs.202040	ESTs; Weakly similar to KIAA0938 protein [H.sapiens]	1.7
	312278	EOS12209	AW205034	Hs.201587	ESTs	1.7
	333368	EOS33289	CH22_804FG_141_9_LINK	EM:AC005500.GENSCAN.21-9	CH22_FGENES.141_9	1.7
30	322735	EOS22868	AA061623	Hs.165803	EST cluster (not in UniGene)	1.7
	326732	EOS26983	c20_hs	g15867615[ref] gn 1 - 1214 1562 ex 2 2 CDS1 33.40 349 1366	CH_20_hs	1.7
	314733	EOS14064	AA542355	Hs.259037	ESTs	1.7
	312902	EOS12833	AW292797	Hs.130316	ESTs	1.7
35	322653	EOS22584	AC828654	Hs.171891	ESTs	1.7
	339015	EOS35946	CH22_3398FG_660_4_LINK	U323110.GENSCAN.9-9	CH22_FGENES.660_4	1.7
	324500	EOS24431	AW298919	Hs.169905	ESTs	1.7
40	310600	EOS10631	CH22_6323FG_LINK	EM:AC005500.GENSCAN.57-1	CH22_FGENES.632_3	1.7
	337908	EOS37839	CH22_6323FG_LINK	EM:AC005500.GENSCAN.57-1	CH22_FGENES.632_3	1.7
	304084	EOS04015	T91986	Hs.191986	EST cluster (not in UniGene) with exon hit	1.7
45	332539	EOS32470	AA412528	Hs.20183	ESTs; Weakly similar to cDNA EST EMBL:TO1421 comes from this gene [C.elegans]	1.7
	314332	EOS14263	AL037551	Hs.95912	ESTs	1.7
	321412	EOS21343	AA369305	Hs.171891	EST cluster (not in UniGene)	1.7
	312187	EOS12118	AA700430	Hs.188490	ESTs	1.7
	314147	EOS14078	AA565135	Hs.129805	ESTs	1.7
50	303131	EOS03062	AW081061	Hs.103180	actin-like 6	1.7
	331341	EOS31272	AA303125	Hs.119009	ESTs; Weakly similar to !!! ALU SUBFAMILY SB2 WARNING ENTRY !!! [H.sapiens]	1.7
	313815	EOS13546	AW295194	Hs.25264	DKFZP434N126 protein	1.7
	329586	EOS29529	c10_p2	g13962482[ref] gn 4 + 39924 40220 ex 2 3 CDS1 8.71 297 420	CH_10_p2	1.7
	303579	EOS03510	AA381124	Hs.195383	ESTs; Weakly similar to !!! ALU SUBFAMILY J WARNING ENTRY !!! [H.sapiens]	1.7
55	331892	EOS16023	W59392	Hs.47343	ESTs	1.7
	323977	EOS23908	CH226177	Hs.234713	ESTs	1.7
	332930	EOS32861	CH22_151FG_38_4_LINK	C20H12.GENSCAN.29-4	CH22_FGENES.38_4	1.7
60	328596	EOS26927	c19_hs	g16138623[ref] gn 4 + 133306 133563 ex 7 9 CDS1 -1.32 178 3520	CH_19_hs	1.7
	314946	EOS14877	A097229	Hs.217484	ESTs; Weakly similar to !!! ALU SUBFAMILY J WARNING ENTRY !!! [H.sapiens]	1.7
	315357	EOS15288	AA068684	Hs.121705	ESTs; Moderately similar to !!! ALU CLASS C WARNING ENTRY !!! [H.sapiens]	1.7
	324728	EOS24859	AA303024	Hs.137007	EST cluster (not in UniGene)	1.7
	317501	EOS14322	AA931245	Hs.139215	ESTs	1.7
65	332915	EOS32150	CH22_2718FG_543_7_LINK	EM:AC005500.GENSCAN.432-9	CH22_FGENES.543_7	1.7
	333589	EOS35300	CH22_2718FG_543_7_LINK	EM:AC005500.GENSCAN.432-9	CH22_FGENES.543_7	1.7
	322417	EOS22548	W36286	Hs.171873	ESTs; Weakly similar to PUTATIVE STEROID DEHYDROGENASE KIK-1 [M.musculus]	1.7
	318100	EOS16031	AW203986	Hs.213003	ESTs	1.7
70	314886	EOS14797	AW305124	Hs.191882	ESTs	1.7
	300328	EOS00259	AW015880	Hs.224623	ESTs	1.7
	315676	EOS15607	AW002565	Hs.139690	ESTs	1.7
	314183	EOS14114	AAT48800	Hs.139690	EST cluster (not in UniGene)	1.7
	321354	EOS21285	AA078493	Hs.139215	EST cluster (not in UniGene)	1.7
	311904	EOS11835	T89907	Hs.119371	ESTs	1.7
75	322890	EOS22821	AA062090	Hs.184727	EST cluster (not in UniGene)	1.7
	302759	EOS02690	A085915	Hs.184727	ESTs	1.7
	304600	EOS24531	AA503297	Hs.117108	ESTs	1.7
	314973	EOS14904	AW273128	Hs.254699	EST	1.7
80	324432	EOS24363	AA464510	Hs.139690	EST cluster (not in UniGene)	1.7
	331520	EOS31451	N49068	Hs.93966	ESTs	1.7
	303390	EOS03311	AW23988	Hs.139690	EST cluster (not in UniGene) with exon hit	1.7
	331010	EOS30941	H95039	Hs.32168	KIAA0442 protein	1.7
	325863	EOS25294	c12_hs	g15869202[ref] gn 7 + 700446 700518 ex 8 8 CDS1 -6.58 71 113	CH_12_hs	1.7
85	310470	EOS10401	AL281948	Hs.165547	ESTs	1.7
	330711	EOS30642	AA184687	Hs.177576	maximosyl (alpha-1,3)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase; isoenzyme A	1.7

5	332074	EOS32005	AA59012	Hs.22826	ESTs	1.6	
	309732	EOS08663	AA262211	Hs.5492	guanine nucleotide binding protein (G protein); beta polypeptide 2-like 1	1.7	
	306337	EOS02628	AA564221	Hs.73742	ribosomal protein; target: P0	1.6	
	335169	EOS36120	CH22_2525FG_507_4_LINK	EM:AC005500.GENSCAN.400-4	CH22_FGENES.507_4	1.6	
10	316253	EOS16184	AI919537	Hs.118096	ESTs	1.6	
	332908	EOS32639	CH22_129FG_36_12_LINK	CC20112.GENSCAN.28-9	CH22_FGENES.36_12	1.6	
	310002	EOS09933	AI439096	Hs.25832	ESTs	1.6	
	332258	EOS32189	N69670	Hs.103808	ESTs; Weakly similar to RanBPM [H.sapiens]	1.6	
15	336182	EOS36113	CH22_3578FG_715_2_LINK	DA598118.GENSCAN.19-3	CH22_FGENES.715_2	1.6	
	328987	EOS28918	c_9_hs	gi 5868535 ref gn 1 - 25705 25764 ex 3 10 CDSI 9.90 60 438	CH109_hs	gi 5868535	1.6
	324481	EOS24412	AI916284	Hs.199671	ESTs	1.6	
	331405	EOS31337	AA610064	Hs.23440	KIAA1105 protein	1.6	
20	332280	EOS32211	R38100	Hs.106294	ESTs	1.6	
	332173	EOS32104	F09281	Hs.90424	ESTs	1.6	
	335739	EOS35670	CH22_3102FG_601_10_LINK	EM:AC005500.GENSCAN.491-10	CH22_FGENES.601_10	1.6	
	332104	EOS32035	AA609177	Hs.109363	ESTs	1.6	
25	315033	EOS14964	AI483046	Hs.146133	ESTs	1.6	
	334740	EOS34671	CH22_2052FG_424_15_LINK	EM:AC005500.GENSCAN.285-17	CH22_FGENES.424_15	1.6	
	334763	EOS34714	CH22_2095FG_432_8_LINK	EM:AC005500.GENSCAN.293-11	CH22_FGENES.432_8	1.6	
	308010	EOS07941	AI439190	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.6	
30	304521	EOS04452	AA464716		EST singleton (not in UniGene) with exon hit	1.6	
	318719	EOS18650	Z25900	Hs.18724	Homo sapiens mRNA; cDNA DKFZp564F093 (from clone DKFZp564F093)	1.6	
	321920	EOS21851	HE3015		EST cluster (not in UniGene)	1.6	
	313519	EOS14950	AA532807	Hs.105822	ESTs	1.6	
35	320793	EOS20724	AL049980	Hs.184216	DKFZP564C152 protein	1.6	
	305371	EOS06302	AA714180		EST singleton (not in UniGene) with exon hit	1.6	
	305054	EOS04085	AA634127	Hs.182426	ribosomal protein S2	1.6	
	314843	EOS14574	AI587502	Hs.192068	ESTs	1.6	
40	306186	EOS08117	AS37940		EST singleton (not in UniGene) with exon hit	1.6	
	319371	EOS19302	R00321	Hs.174928	ESTs	1.6	
	331700	EOS31631	Z40011	Hs.180582	ESTs	1.6	
	318955	EOS18886	AW203859	Hs.149532	ESTs	1.6	
45	314981	EOS14892	AW08081	Hs.231994	ESTs	1.6	
	339676	EOS38607	CH22_4154FG_43_4_LINK	CH22_FGENES.43-4		1.6	
	322801	EOS22732	AI831910	Hs.183734	ESTs	1.6	
	303363	EOS03294	AA694085	Hs.226801	ESTs; Weakly similar to D1A-156 protein [H.sapiens]	1.6	
50	328105	EOS28206	c_8_hs	gi 5868020 ref gn 11 - 301705 301764 ex 4 7 CDSI 5.30 80 3147	CH106_hs	gi 5868020	1.6
	325481	EOS25412	c12_hs	gi 5866957 ref gn 3 + 47500 47672 ex 4 7 CDSI 2.69 83 1895	CH112_hs	gi 5866957	1.6
	315361	EOS15292	AI355229	Hs.122031	ESTs	1.6	
	324902	EOS24633	D31323	Hs.211188	ESTs	1.6	
55	339318	EOS35949	CH22_3401FG_669_7_LINK	DJ32110.GENSCAN.9-12	CH22_FGENES.669_7	1.6	
	308747	EOS08678	AI804500	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.6	
	328251	EOS28182	c_6_hs	gi 5818591 ref gn 4 + 124444 124557 ex 2 3 CDSI 0.40 114 4554	CH106_hs	gi 5818591	1.6
	303153	EOS30304	U09759	Hs.8325	mitogen-activated protein kinase 9	1.6	
60	327809	EOS27740	c_5_hs	gi 5867968 ref gn 3 + 54610 54761 ex 4 4 CDSI 0.78 152 993	CH105_hs	gi 5867968	1.6
	314107	EOS14308	AA806113	Hs.189025	ESTs	1.6	
	303004	EOS09235	AA837934	Hs.224978	ESTs	1.6	
	313009	EOS12940	W52010	Hs.191379	ESTs	1.6	
65	331074	EOS31005	R08440		y1199.s1 Scores fetal liver spleen 1NFLS Homo sapiens cDNA clone IMAGE:127337 3 similar to contains Alu repetitive element; mRNA sequence	1.6	
	335773	EOS35704	CH22_3142FG_607_9_LINK	EM:AC005500.GENSCAN.496-4	CH22_FGENES.607_9	1.6	
	334991	EOS34922	CH22_2312FG_469_11_LINK	EM:AC005500.GENSCAN.365-11	CH22_FGENES.469_11	1.6	
	322959	EOS22890	A0257996		EST cluster (not in UniGene)	1.6	
70	323731	EOS22662	AA323414		EST cluster (not in UniGene)	1.6	
	331073	EOS31004	R07998	Hs.18628	ESTs; Weakly similar to !!! ALU SUBFAMILY J WARNING ENTRY !!! [H.sapiens]	1.6	
	313573	EOS13504	A076259	Hs.190337	ESTs	1.6	
	316949	EOS16880	AA895749	Hs.124620	ESTs	1.6	
75	328084	EOS28015	c_8_hs	gi 5868619 ref gn 9 - 155396 155459 ex 1 4 CDSI 1.23 94 2982	CH106_hs	gi 5868619	1.6
	331526	EOS31457	N49967	Hs.46624	ESTs	1.6	
	317987	EOS17918	AW138174	Hs.130651	ESTs	1.6	
	325594	EOS25625	c13_hs	gi 5868992 ref gn 4 - 470474 470569 ex 2 3 CDSI 8.09 93 68	CH13_hs	gi 5868992	1.6
80	310848	EOS10779	AI459554	Hs.161286	ESTs	1.6	
	302668	EOS08199	AI965821	Hs.62954	ferritin; heavy polypeptide 1	1.6	
	304518	EOS04449	AA461438		EST singleton (not in UniGene) with exon hit	1.6	
	331885	EOS30396	N09584	Hs.9167	Homo sapiens clone Z5065 mRNA sequence	1.6	
85	309561	EOS06432	AA987294		EST singleton (not in UniGene) with exon hit	1.6	
	323899	EOS23220	AL134235	Hs.222442	ESTs	1.6	
	334630	EOS34561	CH22_1938FG_416_8_LINK	EM:AC005500.GENSCAN.277-6	CH22_FGENES.416_8	1.6	
	302325	EOS01956	AI091466	Hs.127241	DKFZP564F052 protein	1.6	

328996	EOS289229	c_9_hs	gi 5866538 ref	gn 1 + 40996 41104 ex 1 3 CDS1 11.00 109 480	1.6
313197	EOS13126	AI238951	Hs.222487	ESTs	1.6
337673	EOS36894	CH22_7585FG_LINK	EM:AC005500.GENSCAN.517-16	CH22_7585FG_LINK	1.6
332247	EOS32176	N56172	Hs.109370	ESTs	1.6
318724	EOS18655	A4810788	Hs.123337	ESTs	1.6
305306	EOS03037	AA215297		EST cluster (not in UniGene) with exon hit	1.6
306336	EOS06267	AA954198		EST singleton (not in UniGene) with exon hit	1.6
308256	EOS08187	AA565498		EST singleton (not in UniGene) with exon hit	1.6
307056	EOS06897	AI148075		EST singleton (not in UniGene) with exon hit	1.6
361370	EOS31301	AJ227900		EST cluster (not in UniGene)	1.6
336262	EOS36193	CH22_3661FG_754_9_LINK	DA59H16.GENSCAN.57-11	CH22_3661FG_754_9_LINK	1.6
335497	EOS35426	CH22_2849FG_571_5_LINK	EM:AC005500.GENSCAN.460-26	CH22_2849FG_571_5_LINK	1.6
309582	EOS06513	AW169657		EST singleton (not in UniGene) with exon hit	1.6
329563	EOS29494	c10_p2	gi 3962490 ga	gn 1 - 410 635 ex 2 2 CDS1 13.80 226 267	1.6
332504	EOS23435	AA053917	Hs.15105	chromosome 14 open reading frame 1	1.6
308050	EOS06021	HA24601	Hs.21166	eukaryotic translation elongation factor 1 gamma	1.6
331782	EOS31683	AA287312	Hs.191648	ESTs	1.6
330881	EOS30812	AA132996	Hs.69321	ESTs; Weakly similar to Smilax to mucin and several other Ser-Thr-rich proteins [S.cerevisiae]	1.6
315647	EOS15578	AA648883	Hs.212911	ESTs	1.6
336766	EOS36897	CH22_4341FG_143_20_	CH22_FGENES.143-20	CH22_FGENES.143-20	1.6
302582	EOS05523	AA034621	Hs.250811	viral human leukemia viral oncogene homolog B (ras related; GTP binding protein)	1.6
315075	EOS15007	AA823817	Hs.168457	ESTs	1.6
337056	EOS36897	CH22_4946FG_441_4_	CH22_FGENES.441-4	CH22_FGENES.441-4	1.6
322175	EOS22106	AF058975		EST cluster (not in UniGene)	1.6
338833	EOS36764	CH22_4504FG_242_2_	CH22_FGENES.242-2	CH22_FGENES.242-2	1.6
334902	EOS34633	CH22_2219FG_452_16_LINK	EM:AC005500.GENSCAN.341-19	CH22_2219FG_452_16_LINK	1.6
318671	EOS18602	AA188823	Hs.212621	ESTs	1.6
308064	EOS07995	AA469273	Hs.181165	eukaryotic translation elongation factor 1 alpha 1	1.6
303559	EOS05490	AB021861	Hs.153322	adipic carrier family 35 (UDP-N-acetylglucosamine (UDP-GlcNAc) transporter); member 3	1.6
317881	EOS17812	AB027148	Hs.153322	ESTs	1.6
331078	EOS13009	AA9730		EST cluster (not in UniGene)	1.6
336889	EOS36820	CH22_7464FG_LINK	EM:AC005500.GENSCAN.475-3	CH22_7464FG_LINK	1.6
311804	EOS11735	AA135159	Hs.203349	ESTs	1.6
316359	EOS18290	AA072213	Hs.123415	ESTs	1.6
330182	EOS30113	c_4_p2	gi 5123954 emb	gn 4 + 120156 120245 ex 2 2 CDS1 4.69 90 11	1.6
334718	EOS34649	CH22_2028FG_421_29_LINK	EM:AC005500.GENSCAN.282-29	CH22_2028FG_421_29_LINK	1.6
324196	EOS24127	AA055624	Hs.176000	ESTs	1.6
305350	EOS06281	AA706876		EST singleton (not in UniGene) with exon hit	1.6
331489	EOS31400	N22273	Hs.39140	ESTs	1.6
363715	EOS05266	AA620684		EST singleton (not in UniGene) with exon hit	1.6
314480	EOS14391	A028231	Hs.145607	ESTs	1.6
317634	EOS17565	AA953088	Hs.127550	ESTs	1.6
332893	EOS35224	CH22_2635FG_527_6_LINK	EM:AC005500.GENSCAN.421-9	CH22_2635FG_527_6_LINK	1.6
305811	EOS05542	AA782331		EST singleton (not in UniGene) with exon hit	1.6
310430	EOS10361	AA070843	Hs.200257	ESTs	1.6
323896	EOS23827	AA641201	Hs.222051	ESTs	1.6
300810	EOS00541	N72596	Hs.99120	DEAD/HH (Arg-Glu-Ala-Asp) box polypeptide, Y chromosome	1.6
327364	EOS27295	c_1_hs	gi 6556212 ref	gn 2 - 116235 115399 ex 1 19 CDS1 2.77 162 3007	1.6
324848	EOS24779	AW021857		EST cluster (not in UniGene)	1.6
321491	EOS21422	H07665	Hs.183960	ESTs	1.6
336367	EOS36298	CH22_3779FG_818_11_LINK	BA232E17.GENSCAN.3-17	CH22_3779FG_818_11_LINK	1.6
331549	EOS31480	N68866	Hs.237507	EST	1.6
328332	EOS28263	c_7_hs	gi 5868379 ref	gn 6 + 260154 280289 ex 3 5 CDS1 -1.04 138 516	1.6
322817	EOS22748	C02420		CH107_hs	gi 5868375
303993	EOS03914	AW514111	Hs.161165	EST cluster (not in UniGene)	1.6
329434	EOS29385	c_y_hs	gi 5868883 ref	gn 1 - 31124 31263 ex 3 20 CDS1 6.38 140 241	1.6
338196	EOS38127	CH22_6783FG_LINK	EM:AC005500.GENSCAN.235-16	CH22_6783FG_LINK	1.6
308488	EOS08419	AA682148	Hs.179961	Homo sapiens clone 24703 beta-tubulin mRNA, complete cds	1.5
314883	EOS14814	AA178807	Hs.246182	ESTs	1.5
307095	EOS07026	AI187910		EST singleton (not in UniGene) with exon hit	1.5
306953	EOS06884	AI124871		EST singleton (not in UniGene) with exon hit	1.5
331786	EOS31717	AA396539	Hs.97369	EST	1.5
303509	EOS03440	AA9378236	Hs.256050	ESTs	1.5
324515	EOS24446	AA050686	Hs.163539	ESTs	1.5
339923	EOS39254	CH22_8284FG_LINK	BA354H12.GENSCAN.23-2	CH22_8284FG_LINK	1.5
306563	EOS06494	AA995296		EST singleton (not in UniGene) with exon hit	1.5
316076	EOS16007	AA0297895	Hs.116424	ESTs	1.5
325822	EOS25553	c14_hs	gi 5867000 ref	gn 2 + 89994 70075 ex 6 8 CDS1 9.40 92 194	1.5
309632	EOS09563	AA193261	Hs.156110	immunoglobulin kappa variable 1D-8	1.5

314926	EOS14857	A130838	Hs.124835	ESTs	1.5
314948	EOS14389	A1217440	Hs.143873	ESTs	1.5
335619	EOS35150	CH22_2558FG_513_2_LINK	EM-AC005500.GENSCAN.406-2	CH22_FGENES.513_2	1.5
301079	EOS01010	A0505047	Hs.139554	ESTs; Weakly similar to unknown [S.cerevisiae]	1.5
334122	EOS34053	CH22_1400FG_333_3_LINK	EM-AC005500.GENSCAN.185-27	CH22_FGENES.333_3	1.5
328139	EOS08070	A494477		EST singleton (not in UniGene) with exon hit	1.5
317412	EOS13743	A1301528	Hs.132604	ESTs	1.5
315073	EOS15004	A1452948	Hs.257031	ESTs	1.5
313139	EOS13070	A4362113		EST cluster (not in UniGene)	1.5
307012	EOS06843	A140212		EST singleton (not in UniGene) with exon hit	1.5
322995	EOS22326	A1470295	Hs.192152	ESTs	1.5
303779	EOS03710	A4897296	Hs.221266	ESTs	1.5
312344	EOS12275	A1742618	Hs.181733	ESTs; Weakly similar to nitrate homolog 1 [H.sapiens]	1.5
323632	EOS23563	A1039950		EST cluster (not in UniGene)	1.5
332336	EOS32257	T95130	Hs.137551	ESTs	1.5
304547	EOS04478	A4088189		EST singleton (not in UniGene) with exon hit	1.5
335692	EOS35623	CH22_3053FG_596_7_LINK	EM-AC005500.GENSCAN.488-7	CH22_FGENES.596_7	1.5
328333	EOS28264	c_7_hs g15868375[ref]	gn 6 + 282505 202604 ex 4 5 CDS: 7.71 159 517	CH107_hs g15868375	1.5
304143	EOS04074	R88737		EST singleton (not in UniGene) with exon hit	1.5
329255	EOS29556	c11_p2 g14567169[gb]A	gn 2 - 85893 85964 ex 3 5 CDS: 2.24 92 29	CH11_p2 g14567169	1.5
329960	EOS28991	c16_p2 g15091594[gb]A	gn 1 - 1031 1162 ex 1 3 CDS: 10.75 132 415	CH16_p2 g15091594	1.5
318975	EOS18906	Z44110		EST cluster (not in UniGene)	1.5
321875	EOS21806	N49122		EST cluster (not in UniGene)	1.5
320451	EOS20382	T26944	Hs.180777	Homo sapiens mRNA; cDNA DKFZp564M0264 (from clone DKFZp564M0264)	1.5
339020	EOS35951	CH22_3403FG_699_9_LINK	EM-AC005500.GENSCAN.5-14	CH22_FGENES.699_9	1.5
332581	EOS32512	T28799	Hs.2913	EphB3	1.5
338622	EOS38553	CH22_7384FG_LINK	EM-AC005500.GENSCAN.451-1	CH22_7384FG_LINK	1.5
330357	EOS30328	D14659	Hs.154387	KIAA0103 gene product	1.5
314359	EOS14290	A1205569	Hs.194193	ESTs	1.5
313456	EOS13387	A1305079	Hs.209557	ESTs	1.5
318486	EOS18417	H09123	Hs.139258	ESTs	1.5
318175	EOS18106	A4844624		EST cluster (not in UniGene)	1.5
335984	EOS35615	CH22_3045FG_595_4_LINK	EM-AC005500.GENSCAN.487-13	CH22_FGENES.595_4	1.5
327814	EOS27745	c_5_hs g15867988[ref]	gn 6 + 89377 70566 ex 1 2 CDS: 86.15 1190 999	CH105_hs g15867988	1.5
322120	EOS22051	W18351	Hs.213846	ESTs	1.5
311749	EOS11680	R05249	Hs.13911	ESTs	1.5
32797	EOS29728	c14_p2 g16523160[emb]	gn 1 - 10616 10894 ex 3 6 CDS: 5.85 279 1549	CH14_p2 g16523160	1.5
330630	EOS30561	X78699	Hs.79088	reticulocalbin 2; EF-hand calcium binding domain	1.5
303777	EOS03708	A3348491		EST cluster (not in UniGene) with exon hit	1.5
309556	EOS05857	AW107080	Hs.195188	glyceraldehyde-3-phosphate dehydrogenase	1.5
329185	EOS28066	c17_hs g15867208[ref]	gn 2 - 62757 62629 ex 1 10 CDS: 0.87 143 2037	CH17_hs g15867208	1.5
306328	EOS02359	A1590571	Hs.186412	EST	1.5
303031	EOS00532	A1762130	Hs.165819	ESTs	1.5
303610	EOS03541	A4323288		EST cluster (not in UniGene) with exon hit	1.5
307856	EOS07787	A1366158		EST singleton (not in UniGene) with exon hit	1.5
319920	EOS11851	R54575	Hs.13337	ESTs; Weakly similar to similar to Phosphoglucosylase and phosphomannomutase phosphoserine (G-degrate)	1.5
32167	EOS32098	D57389	Hs.75447	ralA binding protein 1	1.5
316427	EOS18368	A241019	Hs.145644	ESTs	1.5
303886	EOS03817	AW368963		EST cluster (not in UniGene) with exon hit	1.5
314292	EOS14223	AA732560	Hs.134740	ESTs	1.5
315408	EOS15339	AW72591	Hs.218592	ESTs	1.5
335698	EOS35629	CH22_3058FG_597_1_LINK	EM-AC005500.GENSCAN.489-1	CH22_FGENES.597_1	1.5
315084	EOS15015	A1821085	Hs.187796	ESTs	1.5
322239	EOS02230	R64532	Hs.132167	hemoglobin; gamma A	1.5
306093	EOS06734	A1055860	Hs.193717	interleukin 10	1.5
315802	EOS15733	AA677540	Hs.117064	ESTs	1.5
326257	EOS26188	c17_hs g15867254[ref]	gn 6 + 222712 222819 ex 2 2 CDS: 4.46 108 3597	CH17_hs g15867254	1.5
319599	EOS19530	H56112		EST cluster (not in UniGene)	1.5
321891	EOS21822	AW157424	Hs.169554	ESTs	1.5
335164	EOS35095	CH22_2500FG_502_8_LINK	EM-AC005500.GENSCAN.399-23	CH22_FGENES.502_8	1.5
327133	EOS27064	c21_hs g1682522[ref]	gn 1 + 38269 38258 ex 2 2 CDS: 63.42 870 1583	CH21_hs g1682522	1.5
317480	EOS17391	AA26980	Hs.131347	ESTs	1.5
323444	EOS32275	W45574	Hs.252497	ESTs	1.5
328801	EOS28732	c_7_hs g15868321[ref]	gn 1 - 44492 44609 ex 2 3 CDS: 1.71 118 5525	CH107_hs g15868321	1.5
321877	EOS21608	A44545	Hs.251955	ESTs	1.5
331858	EOS31789	AA421163	Hs.163848	ESTs	1.5
306643	EOS06174	A1972002		EST singleton (not in UniGene) with exon hit	1.5
320213	EOS26144	c17_hs g15867224[ref]	gn 3 - 80751 80627 ex 1 4 CDS: 2.06 177 2687		1.5

			CH.17_hs_gli5867224	1.5		
	321832	EOS21563	AA419617	EST cluster (not in UniGene)	1.5	
	321424	EOS31355	AA057301	EST cluster (not in UniGene)	1.5	
	322465	EOS22396	AA137152	Hs.3784	ESTs; Highly similar to phosphoserine aminotransferase [H.sapiens]	1.5
	333391	EOS33322	CH22_837FG_144_6_LINK_EMAC005500.GENSCAN.25-6	CH22_FGENES.144_6	1.5	
	333384	EOS33315	CH22_836FG_143_23_LINK_EMAC005500.GENSCAN.24-17	CH22_FGENES.143_23	1.5	
	334784	EOS34715	CH22_2096FG_432_9_LINK_EMAC005500.GENSCAN.293-12	CH22_FGENES.432_9	1.5	
	334078	EOS34009	CH22_1366FG_327_33_LINK_EMAC005500.GENSCAN.181-35	CH22_FGENES.327_33	1.5	
	335158	EOS35089	CH22_2494FG_502_2_LINK_EMAC005500.GENSCAN.396-17	CH22_FGENES.502_2	1.5	
	335062	EOS34993	CH22_2388FG_482_17_LINK_EMAC005500.GENSCAN.376-16	CH22_FGENES.482_17	1.5	
	333243	EOS33174	CH22_482FG_111_7_LINK_EMAC000097.GENSCAN.120-6	CH22_FGENES.111_7	1.5	
	306380	EOS06311	AA968861	EST singleton (not in UniGene) with exon hit	1.5	
	320809	EOS20740	A1540299	EST cluster (not in UniGene)	1.5	
	332813	EOS32744	CH22_29FG_8_1_LINK_C06511.GENSCAN.2-2	CH22_FGENES.8_1	1.5	
	335817	EOS35748	CH22_3189FG_618_5_LINK_EMAC005500.GENSCAN.510-5	CH22_FGENES.618_5	1.5	
	319551	EOS19482	AA761688	EST cluster (not in UniGene)	1.5	
	334472	EOS33403	CH22_1771FG_394_3_LINK_EMAC005500.GENSCAN.257-3	CH22_FGENES.394_3	1.5	
	333029	EOS32960	CH22_255FG_68_3_LINK_EMAC000097.GENSCAN.40-3	CH22_FGENES.68_3	1.5	
	320855	EOS07986	AA468091	Hs.119252	tumor protein; translationally-controlled 1	1.5
	320892	EOS02813	AW404330	EST cluster (not in UniGene) with exon hit	1.5	
	314033	EOS13864	AA167125	EST cluster (not in UniGene)	1.5	
	324928	EOS24859	A1932285	Hs.160580	ESTs	1.5
	329524	EOS29455	c10_p2_gli3983507[gb]a gn 6 - 38025 38143 ex 3 3 CDS: 1.40 119 170	CH.10_p2_gli3983507	1.5	
	333131	EOS33062	CH22_360FG_83_6_LINK_EMAC000097.GENSCAN.67-10	CH22_FGENES.83_6	1.5	
	332085	EOS32016	AA600353	Hs.173933	ESTs; Weakly similar to NUCLEAR FACTOR 1X [H.sapiens]	1.5
	305399	EOS06300	AA714400	EST singleton (not in UniGene) with exon hit	1.5	
	300344	EOS00275	AW201487	Hs.213659	ESTs	1.5
	325071	EOS25002	H09993	EST cluster (not in UniGene)	1.5	
	323693	EOS23624	AW297758	Hs.249721	ESTs	1.5
	321899	EOS1830	N55158	Hs.130525	ESTs	1.5
	331857	EOS1788	AA421180	Hs.45458	SWINNF related; matrix associated; actin dependent regulator of chromatin; subfamily x; member 5	1.5
	334850	EOS34781	CH22_2164FG_439_38_LINK_EMAC005500.GENSCAN.311-13	CH22_FGENES.439_38	1.5	
	322810	EOS22541	AF180919	EST cluster (not in UniGene)	1.5	
	335332	EOS35263	CH22_2877FG_535_6_LINK_EMAC005500.GENSCAN.426-6	CH22_FGENES.535_6	1.5	
	307585	EOS07496	AB282468	EST singleton (not in UniGene) with exon hit	1.5	
	314140	EOS14071	AC161473	Hs.154297	ESTs	1.5
	323011	EOS22942	AA580288	EST cluster (not in UniGene)	1.5	
	323386	EOS25297	c12_hs_gli5868920[ref] gn 9 - 302092 92173 ex 1 8 CDS: 15.95 752 187	CH.12_hs_gli5868920	1.5	
	322206	EOS22237	W75935	Hs.145083	ESTs	1.5
	311034	EOS10965	A1564023	Hs.171467	ESTs; Highly similar to NK32-D TYPE II INTEGRAL MEMBRANE PROTEIN [H.sapiens]	1.5
	305881	EOS05012	AA561938	EST singleton (not in UniGene) with exon hit	1.5	
	322933	EOS22864	AA099789	EST cluster (not in UniGene)	1.5	
	335221	EOS35152	CH22_2560FG_513_4_LINK_EMAC005500.GENSCAN.408-4	CH22_FGENES.513_4	1.5	
	304348	EOS04379	AA613107	EST singleton (not in UniGene) with exon hit	1.5	
	334900	EOS34631	CH22_2217FG_452_14_LINK_EMAC005500.GENSCAN.341-17	CH22_FGENES.452_14	1.5	
	318404	EOS18335	A1654108	Hs.135125	ESTs	1.5
	333958	EOS39289	CH22_8328FG_LINK_BA35412.GENSCAN.31-3	CH22_BA35412.GENSCAN.31-3	1.5	
	327074	EOS27005	c21_hs_gli563195[ref] gn 58 + 403993 4040096 ex 3 4 CDS: 0.68 104 1284	CH.21_hs_gli563195	1.5	
	326954	EOS25985	c17_hs_gli5867194[ref] gn 2 - 146342 146489 ex 3 4 CDS: 10.00 128 426	CH.17_hs_gli5867194	1.5	
	326892	EOS26823	c20_hs_gli682511[ref] gn 5 + 119424 119600 ex 29 30 CDS: 18.89 77 2313	CH.20_hs_gli682511	1.5	
	328767	EOS28698	c_7_hs_gli6017031[ref] gn 1 - 35625 35723 ex 4 4 CDS: 5.63 99 5262	CH.07_hs_gli6017031	1.5	
	337772	EOS37703	CH22_8125FG_LINK_EMAC000097.GENSCAN.119-11	CH22_EMAC000097.GENSCAN.119-11	1.5	
	312199	EOS12130	AW438602	Hs.191179	ESTs	1.5
	303906	EOS03437	AA340605	Hs.105887	ESTs	1.5
	325176	EOS05107	TS2843	EST cluster (not in UniGene)	1.5	
	320223	EOS01954	AF060567	Hs.126782	sushi-repeat protein	1.5
	305833	EOS05764	AA857836	Hs.181185	eukaryotic translation elongation factor 1 alpha 1	1.5
	309131	EOS09062	A1929175	Hs.119122	ribosomal protein L13a	1.5
	334184	EOS34115	CH22_1465FG_350_15_LINK_EMAC005500.GENSCAN.209-17	CH22_FGENES.350_15	1.5	
	335188	EOS35119	CH22_2524FG_507_3_LINK_EMAC005500.GENSCAN.400-3	CH22_FGENES.507_3	1.5	

	304813	EOS04744	AA584540	EST singleton (not in UniGene) with exon hit	1.5
	315369	EOS15280	AA808808	Hs.225118 ESTs	1.5
	324434	EOS24365	AA707249	Hs.98789 ESTs	1.5
5	327910	EOS27841	c_8_hs [g5868162]ref	gn 1 + 21822 21748 ex 6 7 CDS1 3.68 127 448 CH.08_hs [g5868162]	1.4
	335671	EOS35602	CH22_3031FG_582_3_LINK	EM:AC005500.GENSCAN.485-4 CH22_FGENES.592_3	1.4
	334943	EOS34874	CH22_2294FG_465_8_LINK	EM:AC005500.GENSCAN.359-8 CH22_FGENES.465_8	1.4
10	328093	EOS26324	c19_hs [g5867341]ref	gn 2 + 41702 41841 ex 5 6 CDS1 20.15 140 504 CH.19_hs [g5867341]	1.4
	302596	EOS05227	AA687181	EST singleton (not in UniGene) with exon hit	1.4
	307243	EOS07174	A1199557	EST singleton (not in UniGene) with exon hit	1.4
	320066	EOS19997	AW364885	Hs.112442 ESTs	1.4
15	311465	EOS11386	A1758660	Hs.2016132 ESTs	1.4
	302822	EOS02753	AW404176	Hs.111611 ribosomal protein L27	1.4
	304987	EOS04918	AA161044	EST singleton (not in UniGene) with exon hit	1.4
	310892	EOS30823	AA149579	Hs.118258 ESTs	1.4
20	333385	EOS33316	CH22_831FG_143_24_LINK	EM:AC005500.GENSCAN.24-18 CH22_FGENES.143_24	1.4
	302828	EOS02557	AB021670	EST cluster (not in UniGene) with exon hit	1.4
	318942	EOS17873	AW294522	Hs.149991 ESTs	1.4
	339361	EOS35292	CH22_8331FG_LINK_BA35412	GENSCAN.32-3 CH22_BA35412.GENSCAN.32-3	1.4
25	309000	EOS08931	A1804489	EST singleton (not in UniGene) with exon hit	1.4
	308004	EOS08335	AA888992	EST singleton (not in UniGene) with exon hit	1.4
	295939	EOS29470	c10_p2 [g3983503]tblU	gn 1 - 1 326 ex 1 3 CDS1 41.66 326 212 CH.10_p2 [g3983503]	1.4
	319663	EOS13594	A1953261	Hs.169813 ESTs	1.4
	323538	EOS23469	AW247998	EST cluster (not in UniGene)	1.4
	337556	EOS37826	CH22_5884FG_LINK_C20H12	GENSCAN.8-1 CH22_C20H12.GENSCAN.8-1	1.4
	303149	EOS00080	AA312995	EST cluster (not in UniGene) with exon hit	1.4
	304484	EOS08415	A1879232	EST singleton (not in UniGene)	1.4
35	300912	EOS02843	A1113724	Hs.168974 ESTs	1.4
	315158	EOS15089	AA744438	Hs.142476 ESTs; Weakly similar to [H] ALU CLASS D WARNING ENTRY [H] [H.sapiens]	1.4
	300462	EOS00393	AA746501	Hs.142117 ESTs	1.4
	312730	EOS12661	A1804372	Hs.208661 ESTs	1.4
	316568	EOS16789	A1606808	Hs.195002 ESTs	1.4
40	337529	EOS37560	CH22_5939FG_LINK_C20H12	GENSCAN.28-35 CH22_C20H12.GENSCAN.28-35	1.4
	332518	EOS32449	D16562	Hs.155433 ATP synthase, H+ transporting; mitochondrial F1 complex; gamma polypeptide 1	1.4
	337422	EOS37353	CH22_5824FG_780_2	CH22_FGENES.760-2 c_7_hs [g5865339]ref	gn 1 + 68853 88461 ex 3 3 CDS1 13.78 409 5775
45	328635	EOS23766	c_7_hs [g5865339]ref	gn 1 + 68853 88461 ex 3 3 CDS1 13.78 409 5775 CH.07_hs [g5865339]	1.4
	338282	EOS38213	CH22_6897FG_LINK_EM:AC005500	GENSCAN.291-4 CH22_EM:AC005500.GENSCAN.291-4	1.4
	337895	EOS37826	CH22_6309FG_LINK_EM:AC005500	GENSCAN.59-2 CH22_EM:AC005500.GENSCAN.59-2	1.4
	200330	EOS20261	AF026004	Hs.141660 chloride channel 2	1.4
	314302	EOS14233	AA813118	Hs.163230 ESTs	1.4
	313280	EOS13211	AD955537	Hs.222830 ESTs	1.4
	333222	EOS33153	CH22_459FG_105_2_LINK	EM:AC000097.GENSCAN.109-6 CH22_FGENES.105_2	1.4
55	305726	EOS05557	AA828156	EST singleton (not in UniGene) with exon hit	1.4
	312874	EOS12605	A1760475	Hs.151327 ESTs; Moderately similar to [H] ALU SUBFAMILY J WARNING ENTRY [H] [H.sapiens]	1.4
	315989	EOS15840	A0325447	Hs.122826 ESTs	1.4
	327010	EOS26941	c21_hs [g5867694]ref	gn 12 + 941557 941139 ex 9 9 CDS1 7.44 83 790 CH.21_hs [g5867694]	1.4
60	325992	EOS25823	c16_hs [g5867088]ref	gn 1 - 10498 10652 ex 2 3 CDS1 3.94 155 870 CH.16_hs [g5867088]	1.4
	302575	EOS02506	AF071164	Hs.249171 homeo box 4.11	1.4
	301970	EOS01901	AB028992	Hs.120245 KIAA1039 protein	1.4
	332007	EOS32138	H81475	Hs.237953 EST	1.4
65	318024	EOS15595	AA707141	Hs.193388 ESTs	1.4
	314599	EOS14530	AW200512	Hs.168996 ESTs	1.4
	333585	EOS33516	CH22_848FG_202_4_LINK	EM:AC005500.GENSCAN.74-6 CH22_FGENES.203_4	1.4
	324670	EOS24601	A1525557	EST cluster (not in UniGene)	1.4
	321307	EOS32138	R81549	EST cluster (not in UniGene)	1.4
70	335170	EOS35101	CH22_2506FG_500_1_LINK	EM:AC005500.GENSCAN.397-1 CH22_FGENES.503_1	1.4
	328274	EOS28205	c_7_hs [g5868219]ref	gn 2 - 31244 31439 ex 1 11 CDS1 13.06 196 9 CH.07_hs [g5868219]	1.4
75	335880	EOS36811	CH22_4618FG_318_8	CH22_FGENES.318-8 CH22_FGENES.318-8	1.4
	313825	EOS13766	AA215470	EST cluster (not in UniGene)	1.4
	318410	EOS18341	A1138418	Hs.144835 ESTs	1.4
	335361	EOS33292	CH22_2710FG_541_11_LINK	EM:AC005500.GENSCAN.431-16 CH22_FGENES.541_11	1.4
80	319802	EOS19733	A1701489	Hs.202501 ESTs	1.4
	334769	EOS34700	CH22_2081FG_429_4_LINK	EM:AC005500.GENSCAN.280-9 CH22_FGENES.429_4	1.4
	312709	EOS12640	AW069181	Hs.141148 ESTs; Weakly similar to transformation-related protein [H.sapiens]	1.4
85	330004	EOS29935	c16_p2 [g6823963]tbla	gn 5 - 78872 78959 ex 2 6 CDS1 19.93 128 728 CH.16_p2 [g6823963]	1.4
	313103	EOS13034	A1184303	Hs.143806 ESTs	1.4

5	326359	EOS26290	c18_hs gl 5867293 ref gn 1 + 9436 9484 ex 2 3 CDS1 2.16 59 88	CH.18_hs gl 5867293	1.4	
	305211	EOS95142	AA688563	EST singleton (not in UniGene) with exon hit	1.4	
	334628	EOS34559	CH22_1936FG_416_4_LINK_EM-AC005500.GENSCAN.277-4	CH22_FGENES.416_4	1.4	
10	326919	EOS26850	c21_hs gl 6456782 ref gn 2 - 40486 41046 ex 1 5 CDS1 17.70 561 157	CH.21_hs gl 6456782	1.4	
	315627	EOS15458	A791138	ESTs	1.4	
	306090	EOS06021	AA080809	EST singleton (not in UniGene) with exon hit	1.4	
15	303316	EOS03247	AF033122	Ha.14125 p63 regulated PA26 nuclear protein	1.4	
	303642	EOS03573	AW299458	EST cluster (not in UniGene) with exon hit	1.4	
	314357	EOS14288	AA781795	ESTs	1.4	
20	337102	EOS07033	CH22_5035FG_472_7_LINK	CH22_FGENES.472-7	1.4	
	304384	EOS04315	AA235482	Ha.62954 lefmin; heavy polypeptide 1	1.4	
	315117	EOS15048	AA828609	ESTs	1.4	
25	307570	EOS05681	AA835250	EST singleton (not in UniGene) with exon hit	1.4	
	311726	EOS11657	AW081766	Ha.253920	ESTs	1.4
	326595	EOS26927	c21_hs gl 5867660 ref gn 4 - 83212 83404 ex 2 6 CDS1 15.70 193 822	CH.21_hs gl 5867660	1.4	
30	330257	EOS30188	c_5_p2 gl 6671881 gb A gn 2 - 143228 143393 ex 1 9 CDS1 11.31 166 586	CH.05_p2 gl 6671881	1.4	
	323864	EOS23795	AA340724	ESTs	1.4	
	338204	EOS38135	CH22_6773FG_LINK_EM-AC005500.GENSCAN.241-3	CH22_EM-AC005500.GENSCAN.241-3	1.4	
35	314025	EOS13956	A983981	Ha.189114	ESTs	1.4
	315874	EOS15905	AW029203	Ha.191952	ESTs	1.4
	335599	EOS31530	CH22_2367FG_581_39_LINK_EM-AC005500.GENSCAN.476-37	CH22_FGENES.581_39	1.4	
40	335364	EOS35295	CH22_2713FG_543_2_LINK_EM-AC005500.GENSCAN.432-4	CH22_FGENES.543_2	1.4	
	309364	EOS03665	A953377	Ha.169425	ESTs; Weakly similar to predicted using GeneFinder [C.elegans]	1.4
	315626	EOS15557	AA080598	Ha.35353	ESTs; Weakly similar to H21P03.2 [C.elegans]	1.4
45	329936	EOS29867	c16_p2 gl 6165200 gb A gn 4 - 82761 82820 ex 3 4 CDS1 1.15 190 199	CH.16_p2 gl 6165200	1.4	
	329632	EOS28563	c_7_hs gl 5868247 ref gn 1 + 78734 78553 ex 1 4 CDS1 13.95 120 374	CH.07_hs gl 5868247	1.4	
	330207	EOS30138	c_5_p2 gl 601360 gb A gn 3 - 109912 110004 ex 2 4 CDS1 6.54 93 174	CH.05_p2 gl 601360	1.4	
50	329919	EOS29850	c16_p2 gl 6223624 gb A gn 6 - 103492 103681 ex 1 8 CDS1 6.18 190 93	CH.16_p2 gl 6223624	1.4	
	331916	EOS31847	AA446131	Ha.124918	ESTs	1.4
	317617	EOS17548	T58194	EST cluster (not in UniGene)	1.4	
55	331943	EOS31874	AA453418	Ha.176272	ESTs	1.4
	306413	EOS06344	AA973289	EST singleton (not in UniGene) with exon hit	1.4	
	313907	EOS13538	N94169	Ha.194259	ESTs; Moderately similar to III [ALU SUBFAMILY SC WARNING ENTRY !!!] [H.sapiens]	1.4
60	336292	EOS36223	CH22_3691FG_783_3_LINK_BA354H12.GENSCAN.4-7	CH22_FGENES.783_3	1.4	
	330453	EOS03084	HQ3978-HT4246	Pos-Domain Dna Binding Factor P11, Plutary-Specific	1.4	
	324602	EOS24533	AA503820	Ha.213239	ESTs	1.4
65	332183	EOS32114	H08225	Ha.177181	ESTs	1.4
	320032	EOS19963	AI699772	Ha.202361	ESTs; Weakly similar to X-linked retinopathy protein [H.sapiens]	1.4
	333156	EOS33087	CH22_387FG_69_6_LINK_EM-AC000397.GENSCAN.84-8	CH22_FGENES.89_6	1.4	
70	334156	EOS34087	CH22_1435FG_340_8_LINK_EM-AC005500.GENSCAN.190-7	CH22_FGENES.340_8	1.4	
	334303	EOS34234	CH22_1594FG_373_6_LINK_EM-AC005500.GENSCAN.233-5	CH22_FGENES.373_6	1.4	
	325513	EOS25444	c12_hs gl 8017035 ref gn 1 - 34295 34490 ex 2 7 CDS1 6.49 196 2471	CH.12_hs gl 8017035	1.4	
75	302759	EOS02689	AA984563	EST cluster (not in UniGene) with exon hit	1.4	
	329557	EOS25498	c10_p2 gl 39682482 gb A gn 6 - 53167 53847 ex 2 2 CDS1 37.69 451 247	CH.10_p2 gl 39682482	1.4	
	331717	EOS31648	AA190888	Ha.153081	ESTs; Highly similar to NY-FEN-62 antigen [H.sapiens]	1.4
80	325875	EOS25616	c16_hs gl 5867087 ref gn 11 + 193212 193377 ex 1 3 CDS1 43.19 166 792	CH.16_hs gl 5867087	1.4	
	312160	EOS12091	AA080903	Ha.184371	ESTs	1.4
	328882	EOS28813	c_7_hs gl 6552423 ref gn 2 - 157669 157826 ex 4 6 CDS1 4.91 158 6200	CH.07_hs gl 6552423	1.4	
85	339028	EOS38959	CH22_7925FG_LINK_DA59H18.GENSCAN.22-8	CH22_DA59H18.GENSCAN.22-8	1.4	
	323497	EOS23426	A1523613	Ha.221544	ESTs	1.4
	316897	EOS16828	AA838114	EST cluster (not in UniGene)	1.4	
90	312479	EOS12410	AI860844	Ha.126738	ESTs; Weakly similar to non-lens beta gamma-crystallin like protein [H.sapiens]	1.4
	336535	EOS38466	CH22_725FG_LINK_EM-AC005500.GENSCAN.404-3	CH22_EM-AC005500.GENSCAN.404-3	1.4	
	312754	EOS12665	R98934	Ha.250383	ESTs	1.4
95	327527	EOS25745	c_2_hs gl 6381882 ref gn 2 - 89950 99040 ex 4 8 CDS1 5.79 91 1768	CH.02_hs gl 6381882	1.4	
	324714	EOS24645	AA574312	Ha.245737	ESTs	1.4
	302347	EOS02276	AF939400	Ha.194659	ion channel; calcium activated; family member 1	1.4
100	338008	EOS37939	CH22_6490FG_LINK_EM-AC005500.GENSCAN.127-9	CH22_EM-AC005500.GENSCAN.127-9	1.4	
	315590	EOS15521	AA640637	Ha.225817	ESTs	1.4
	320825	EOS20756	NM_004751	EST cluster (not in UniGene)	1.4	
105	300930	EOS00861	AI289481	Ha.136371	ESTs	1.4
	336225	EOS35156	CH22_254FG_513_10_LINK_EM-AC005500.GENSCAN.406-9		1.4	

				CH22_FGENES.513_10	1.4
				CH22_FGENES.681-5	1.4
	337303	EO537234	CH22_5442FG_681_5	ESTs	1.4
	317198	EO517129	AI810384	EST singleton (not in UniGene) with exon hit	1.4
	308991	EO508622	AI679831	EST singleton (not in UniGene) with exon hit	1.4
5	325472	EO525403	c12_hs gj[6017034]/ref gn 7 - 289581 289657 ex 2 6 CDS1 4.74 77 1786	CH.12_hs gj[6017034]	1.4
				EST cluster (not in UniGene) with exon hit	1.4
	301266	EO501197	AA829774	Human endogenous retroviral protease mRNA; complete cds	1.4
	333601	EO530832	AA157818	ESTs	1.4
	313406	EO513337	EA248314	ESTs	1.4
10	301454	EO501385	A1751738	EST cluster (not in UniGene) with exon hit	1.4
	317269	EO517200	AA906411	ESTs	1.4
	335676	EO535607	CH22_7733FG_LINK_DJ5210.GENSCAN.4-2	CH22_DJ5210.GENSCAN.4-2	1.4
				CH22_DJ5210.GENSCAN.4-2	1.4
15	328481	EO528412	c_7_hs gj[5868449]/ref gn 1 - 8687 9180 ex 4 31 CDS1 10.00 194 2103	CH.07_hs gj[5868449]	1.4
				ESTs	1.4
	314022	EO513853	AW452420	EST singleton (not in UniGene) with exon hit	1.4
	307614	EO507571	AA151992	ESTs; Weakly similar to KIAA0668 protein [H.sapiens]	1.4
	315541	EO515472	AI168233	ESTs	1.4
	315489	EO515420	AA828245	ESTs	1.4
20	327815	EO527746	c_5_hs gj[5867968]/ref gn 6 + 70904 71401 ex 2 2 CDS1 27.99 598 1000	CH.05_hs gj[5867968]	1.4
				CH22_8280FG_LINK_BA35412.GENSCAN.22-19	1.4
	336319	EO536250	CH22_8280FG_LINK_BA35412.GENSCAN.22-19	CH22_8280FG_LINK_BA35412.GENSCAN.22-19	1.4
				ESTs	1.4
25	322584	EO522495	W86440	ESTs	1.4
	322612	EO523743	AW081373	ESTs	1.4
	303540	EO503471	AA356807	ESTs; Weakly similar to MMSET type I [H.sapiens]	1.4
	337902	EO537833	CH22_6314FG_LINK_EM-AC005500.GENSCAN.56-13	CH22_EM-AC005500.GENSCAN.56-13	1.4
				CH22_6314FG_LINK_EM-AC005500.GENSCAN.56-13	1.4
30	335289	EO532220	CH22_2631FG_627_2_LINK_EM-AC005500.GENSCAN.421-2	CH22_FGENES.527_2	1.4
				CH22_FGENES.527_2	1.4
	327919	EO527850	c_6_hs gj[5868165]/ref gn 6 + 547701 547800 ex 14 14 CDS1 -0.20 100 505	CH.06_hs gj[5868165]	1.4
				CH22_6005FG_LINK_EM-AC000097.GENSCAN.67-4	1.4
35	337674	EO537605	CH22_6005FG_LINK_EM-AC000097.GENSCAN.67-4	CH22_6005FG_LINK_EM-AC000097.GENSCAN.67-4	1.4
				small nuclear RNA activating complex; polypeptide 4; 190kd	1.4
	320087	EO520018	AF332367	ESTs	1.3
	334939	EO534670	CH22_2259FG_465_3_LINK_EM-AC005500.GENSCAN.355-3	CH22_FGENES.465_3	1.4
				EST cluster (not in UniGene) with exon hit	1.3
40	303443	EO503374	AA320525	EST cluster (not in UniGene) with exon hit	1.3
	329529	EO525860	c16_hs gj[5867125]/ref gn 2 - 51715 51946 ex 1 1 CDS0 29.05 262 1594	CH.16_hs gj[5867125]	1.3
				CH.05_hs gj[5863159]/ref gn 1 - 229066 229124 ex 3 6 CDS1 3.01 59 177	1.3
	327745	EO527676	c_5_hs gj[5863159]/ref gn 1 - 229066 229124 ex 3 6 CDS1 3.01 59 177	CH.05_hs gj[5863159]	1.3
				CH22_2502FG_502_10_LINK_EM-AC005500.GENSCAN.396-25	1.3
45	335166	EO535097	CH22_2502FG_502_10_LINK_EM-AC005500.GENSCAN.396-25	CH22_FGENES.502_10	1.3
				ESTs	1.3
	324497	EO524426	AW152624	ESTs	1.3
	338374	EO538305	CH22_7017FG_LINK_EM-AC005500.GENSCAN.327-1	CH22_EM-AC005500.GENSCAN.327-1	1.3
				ESTs	1.3
50	313601	EO513632	R32458	Transmembrane 4 superfamily member 1	1.3
	321415	EO521346	AI377598	EST singleton (not in UniGene) with exon hit	1.3
	305306	EO505240	AA698717	Pre-Mrna Splicing Factor S2p33, All Splice Form 1	1.3
	330447	EO530378	HG3546-HT3744	EST singleton (not in UniGene) with exon hit	1.3
	308578	EO508609	AF108573	ESTs	1.3
	315244	EO515275	AW292176	Human cell surface glycoprotein P3.58 mRNA, partial cds	1.3
55	330503	EO530434	M55024	glyceraldehyde-3-phosphate dehydrogenase	1.3
	308227	EO508158	AI559126	ESTs	1.3
	332222	EO532153	N92871	ESTs	1.3
	323291	EO523862	AL044428	ESTs	1.3
	314530	EO514461	AI062358	ESTs	1.3
	320503	EO520434	NM_005897	EST cluster (not in UniGene)	1.3
60	306820	EO506751	AF074408	EST singleton (not in UniGene) with exon hit	1.3
	304165	EO504096	AF3285	EST singleton (not in UniGene) with exon hit	1.3
	324392	EO524233	AA543008	ESTs; Weakly similar to IIIA ALU SUBFAMILY J WARNING ENTRY III [H.sapiens]	1.3
	319128	EO519059	AA393820	EST cluster (not in UniGene)	1.3
	317092	EO517023	AI286162	ESTs	1.3
65	304998	EO504989	AA621203	EST singleton (not in UniGene) with exon hit	1.3
	313433	EO513364	H61807	EST	1.3
	333348	EO533279	CH22_594FG_140_2_LINK_EM-AC005500.GENSCAN.20-2	CH22_FGENES.140_2	1.3
				CH22_FGENES.219_3	1.3
70	333619	EO533650	CH22_860FG_219_3_LINK_EM-AC005500.GENSCAN.67-2	CH22_FGENES.219_3	1.3
	333603	EO533634	CH22_3280FG_635_11_LINK_EM-AC005500.GENSCAN.625-14	CH22_FGENES.635_11	1.3
				CH22_FGENES.635_11	1.3
	326219	EO526150	c17_hs gj[5867226]/ref gn 11 - 264008 264274 ex 3 5 CDS1 5.74 267 2847	CH.17_hs gj[5867226]	1.3
75				EST cluster (not in UniGene)	1.3
	324456	EO524367	AW500954	ESTs	1.3
	316405	EO516336	AA757900	ESTs	1.3
	314391	EO514292	AL038765	ESTs	1.3
	328646	EO528777	c_7_hs gj[5868487]/ref gn 1 - 17547 17722 ex 2 3 CDS1 9.96 176 3284	CH.07_hs gj[5868487]	1.3
80				CH22_3246FG_629_19_LINK_EM-AC005500.GENSCAN.519-18	1.3
				CH22_FGENES.629_19	1.3
	303735	EO503666	AA707750	ESTs; Weakly similar to cis-Go/g matrix protein GM130 [R. norvegicus]	1.3
	304548	EO502979	AF3285	EST cluster (not in UniGene)	1.3
85	326729	EO526651	c20_hs gj[6552456]/ref gn 1 + 84525 84677 ex 5 7 CDS1 11.78 153 1031	CH.20_hs gj[6552456]	1.3
				EST cluster (not in UniGene)	1.3
	322309	EO522240	AF086372	EST cluster (not in UniGene)	1.3

322136	EOS22067	AF075083	EST cluster (not in UniGene)	1.3
313460	EOS13391	AW028655	Hs.136033 ESTs	1.3
306275	EOS06206	AA338312	EST singleton (not in UniGene) with exon hit	1.3
321974	EOS21905	NT67394	EST cluster (not in UniGene)	1.3
327950	EOS27531	c_3_hs_g[6004482]ref gn 1 - 2621 2862 ex 1 4 CDS1 -4.01 242 1407	CH.03_hs_g[6004482]	1.3
329086	EOS29017	c_x_hs_g[5868604]ref gn 1 - 35489 35588 ex 2 9 CDS1 2.55 100 719	CH.X_hs_g[5868604]	1.3
336919	EOS36850	CH22_4680FG_346_8	CH22_FGENES.346_8	1.3
302767	EOS02698	H94900	Hs.17882 ESTs	1.3
334786	EOS34717	CH22_208FG_432_11_LINK	EM:AC005500.GENSCAN.293-14	1.3
302472	EOS02403	AA317451	CH22_FGENES.432_11	1.3
333033	EOS32964	CH22_259FG_68_8_LINK	EM:AC000097.GENSCAN.40-8	1.3
330493	EOS30424	M27826	CH22_FGENES.68_8	1.3
335506	EOS30437	M61993	Human endogenous retroviral protease mRNA; complete cds	1.3
313932	EOS13863	AI147901	phosphorinoside-3-kinase, regulatory subunit; polypeptide 1 (p85 alpha)	1.3
314394	EOS14325	AI080563	ESTs	1.3
323033	EOS22964	AI744284	ESTs	1.3
326431	EOS26362	c19_hs_g[5867371]ref gn 1 + 15855 15971 ex 4 6 CDS1 7.79 117 1108	CH19_hs_g[5867371]	1.3
335547	EOS35478	CH22_2902FG_576_8_LINK	EM:AC005500.GENSCAN.467-8	1.3
300548	EOS00479	AI026538	CH22_FGENES.576_8	1.3
315504	EOS16435	AW135654	ESTs	1.3
335756	EOS35687	CH22_3123FG_604_5_LINK	EM:AC005500.GENSCAN.493-10	1.3
301209	EOS01140	AI080912	CH22_FGENES.604_5	1.3
306510	EOS05541	AI000535	ESTs	1.3
314439	EOS14370	AI59443	EST singleton (not in UniGene) with exon hit	1.3
315396	EOS15327	AW296107	ESTs	1.3
335914	EOS35845	CH22_3291FG_636_10_LINK	EM:AC005500.GENSCAN.526-10	1.3
333734	EOS33655	CH22_1000FG_260_2_LINK	CH22_FGENES.636_10	1.3
312370	EOS12301	AA744892	CH22_FGENES.260_2	1.3
304636	EOS04567	AA524031	ESTs	1.3
323166	EOS20367	AA291001	EST singleton (not in UniGene) with exon hit	1.3
336702	EOS33653	CH22_7482FG_LINK	EM:AC005500.GENSCAN.480-1	1.3
322331	EOS22282	AF086467	EST cluster (not in UniGene)	1.3
318706	EOS18637	AI093593	ESTs	1.3
331181	EOS33117	T41159	Hs.18418 ESTs	1.3
334764	EOS34895	CH22_2078FG_128_13_LINK	EM:AC005500.GENSCAN.289-13	1.3
327565	EOS27496	c_3_hs_g[5867811]ref gn 1 + 32516 32778 ex 2 3 CDS1 0.20 263 358	CH22_FGENES.428_13	1.3
335524	EOS35455	CH22_2878FG_572_4_LINK	CH22_FGENES.572_4	1.3
308050	EOS07981	AI480004	EST singleton (not in UniGene) with exon hit	1.3
334172	EOS34103	CH22_1482FG_348_5_LINK	EM:AC005500.GENSCAN.298-6	1.3
315674	EOS15605	AA851923	CH22_FGENES.348_5	1.3
334878	EOS34807	CH22_2190FG_450_6_LINK	EM:AC005500.GENSCAN.339-6	1.3
315606	EOS15537	AW298724	CH22_FGENES.450_6	1.3
338779	EOS38710	CH22_7610FG_LINK	EM:AC005500.GENSCAN.526-15	1.3
333511	EOS33442	CH22_766FG_171_5_LINK	CH22_FGENES.171_5	1.3
329254	EOS29165	c_x_hs_g[5868733]ref gn 1 + 4133 4214 ex 1 2 CDS1 -0.36 82 2833	CH.X_hs_g[5868733]	1.3
319510	EOS18441	W88633	Hs.254582 ESTs	1.3
339418	EOS39349	CH22_8411FG_LINK	EM:AC005500.GENSCAN.11-4	1.3
321012	EOS20943	AA737314	CH22_D879W18	1.3
333217	EOS33148	CH22_454FG_104_9_LINK	EM:AC000097.GENSCAN.106-8	1.3
338561	EOS38492	CH22_7294FG_LINK	CH22_FGENES.104_9	1.3
335742	EOS35673	CH22_3105FG_601_13_LINK	EM:AC005500.GENSCAN.421-5	1.3
334993	EOS34924	CH22_2314FG_469_14_LINK	CH22_FGENES.469_14	1.3
323430	EOS23361	AW062479	EST cluster (not in UniGene)	1.3
306069	EOS06000	AA506983	EST singleton (not in UniGene) with exon hit	1.3
331681	EOS31612	W85712	collagen, type III; alpha 1 (Ehlers-Danlos syndrome type IV; autosomal dominant)	1.3
337986	EOS37917	CH22_8441FG_LINK	EM:AC005500.GENSCAN.110-7	1.3
313204	EOS13135	AI080518	CH22_FGENES.110-7	1.3
323189	EOS23120	AL121184	ESTs	1.3
318171	EOS18162	AA381632	EST cluster (not in UniGene)	1.3
307156	EOS07087	AI186762	EST singleton (not in UniGene) with exon hit	1.3
332713	EOS32844	AA349792	multY (E. coli) homolog	1.3
312828	EOS12759	AB05455	ESTs; Moderately similar to Hs.211818	1.3

	339132	EOS36063	CH22_3522FG_703_2_LINK_DA59H18.GENSCAN.9-2		
			CH22_FGENES.703_2		1.3
	337958	EOS37869	CH22_6403FG_LINK_EM.AC005500.GENSCAN.98-6		
			CH22_EM.AC005500.GENSCAN.98-6		1.3
5	305630	EOS05561	AA804508	EST singleton (not in UniGene) with exon hit	1.3
	334916	EOS34847	CH22_2235FG_457_7_LINK_EM.AC005500.GENSCAN.347-1		
			CH22_FGENES.457_7		1.3
	333542	EOS33473	CH22_799FG_178_4_LINK_EM.AC005500.GENSCAN.59-4		
			CH22_FGENES.178_4		1.3
10	331151	EOS31082	R82331	Hs.164599	ESTs
	315095	EOS15025	AA891815	Hs.243788	ESTs
	331583	EOS31524	N72150	Hs.50193	EST
	323787	EOS32688	AA807408	Hs.163688	ESTs
	334561	EOS34492	CH22_1865FG_405_1_LINK_EM.AC005500.GENSCAN.270-5		
			CH22_FGENES.405_1		1.3
15	308191	EOS08122	A153878	EST singleton (not in UniGene) with exon hit	1.3
	319571	EOS19522	N91399	Hs.220835	ESTs
	316200	EOS16131	A1914535	Hs.221977	ESTs
	305996	EOS05927	AA889338	Hs.163356	EST
20	318055	EOS17988	A249183	Hs.145945	ESTs
	315570	EOS15501	A1680360	Hs.160316	ESTs
	320792	EOS20723	AW236504	Hs.247020	ESTs
	331649	EOS31580	W20364	Hs.55412	ESTs; Weakly similar to c29 [M.musculus]
	303839	EOS03770	Z45939		EST cluster (not in UniGene) with exon hit
25	324399	EOS24330	AA814768	Hs.21396	ESTs
	317172	EOS17103	AT741232	Hs.200744	ESTs
	312452	EOS12383	A682643	Hs.172749	ESTs
	325482	EOS25413	c12_hs_g1586957[ref] gn 3 + 47957 48078 ex 5 7 CDS1 10.25 122 1886		1.2
30	311365	EOS11326	R23313	CH.12_hs_g1586957	1.2
	336124	EOS36065	CH22_3513FG_701_9_LINK_DA59H18.GENSCAN.8-9		
			CH22_FGENES.701_9		1.2
	320082	EOS20013	AA467678	Hs.189738	ESTs
	321688	EOS12699	T22551	Hs.198882	ESTs
35	339000	EOS37851	CH22_6472FG_LINK_EM.AC005500.GENSCAN.119-5		
			CH22_EM.AC005500.GENSCAN.119-5		1.2
	338852	EOS38783	CH22_7705FG_LINK_D124607.GENSCAN.12-1		
			CH22_D124607.GENSCAN.12-1		1.2
40	312090	EOS12021	N57692	Hs.118064	ESTs
	316480	EOS16411	A748921	Hs.205377	ESTs
	333259	EOS33190	CH22_500FG_118_7_LINK_EM.AC005500.GENSCAN.2-7		
			CH22_FGENES.118_7		1.2
	335211	EOS35142	CH22_2550FG_511_2_LINK_EM.AC005500.GENSCAN.403-2		
			CH22_FGENES.511_2		1.2
45	321950	EOS21881	AA584780	Hs.172318	ESTs
	337937	EOS37868	CH22_6370FG_LINK_EM.AC005500.GENSCAN.86-1		
			CH22_EM.AC005500.GENSCAN.86-1		1.2
	316576	EOS16507	A732114	Hs.193046	ESTs; Weakly similar to [Hsapiens]
50	322770	EOS22701	AA045796	Hs.159971	SWI/SNF related; matrix associated; actin dependent regulator of chromatin; subfamily b; member 1
	329369	EOS29300	c_x_hs_g15868842[ref] gn 1 - 121148 121516 ex 3 4 CDS1 8.50 369 3910		1.2
			CH.X_hs_g15868842		1.2
	304183	EOS04114	H81161	EST singleton (not in UniGene) with exon hit	1.2
	339370	EOS39301	CH22_8343FG_LINK_BA232E17.GENSCAN.1-12		
			CH22_BA232E17.GENSCAN.1-12		1.2
55	303941	EOS03872	AW473878	Hs.156110	Immunoglobulin kappa variable 1D-8
	302245	EOS02176	H18805	EST cluster (not in UniGene) with exon hit	1.2
	332555	EOS35186	CH22_2397FG_517_2_LINK_EM.AC005500.GENSCAN.411-2		
			CH22_FGENES.517_2		1.2
60	316610	EOS16541	AW087873	Hs.126731	ESTs
	314915	EOS14846	AA573072	Hs.187748	ESTs; Weakly similar to [Hsapiens]
	315426	EOS15557	A1991489	Hs.128117	ESTs
	334003	EOS33354	CH22_1281FG_310_28_LINK_EM.AC005500.GENSCAN.167-27		
			CH22_FGENES.310_28		1.2
65	304350	EOS04281	AA186871		EST singleton (not in UniGene) with exon hit
	325173	EOS15104	A1132115	Hs.144682	ESTs; Moderately similar to [Hsapiens]
	312313	EOS12244	AW293341	Hs.122650	ESTs
	333386	EOS33297	CH22_612FG_142_3_LINK_EM.AC005500.GENSCAN.22-6		
			CH22_FGENES.142_3		1.2
70	334970	EOS34901	CH22_2291FG_466_3_LINK_EM.AC005500.GENSCAN.361-2		
			CH22_FGENES.466_3		1.2
	338668	EOS38599	CH22_7441FG_LINK_EM.AC005500.GENSCAN.465-1		
			CH22_EM.AC005500.GENSCAN.465-1		1.2
	336502	EOS36433	CH22_3926FG_833_9_LINK_D1579H16.GENSCAN.5-9		
			CH22_FGENES.833_9		1.2
75	309438	EOS09369	AW102802	Hs.225767	ESTs; Moderately similar to hypothetical protein [Hsapiens]
	336194	EOS36125	CH22_3591FG_717_20_LINK_DA59H18.GENSCAN.20-19		
			CH22_FGENES.717_20		1.2
	309978	EOS36609	CH22_4159FG_Q3_8		CH22_FGENES.43-6
	321401	EOS21332	W90406	Hs.35962	ESTs
80	306026	EOS05957	AA902309		EST singleton (not in UniGene) with exon hit
	336434	EOS36365	CH22_3854FG_826_1_LINK_BA232E17.GENSCAN.8-1		
			CH22_FGENES.826_1		1.2
	315257	EOS15158	AW157431	Hs.248941	ESTs
	328349	EOS28280	c_7_hs_g15868383[ref] gn 7 - 260704 260804 ex 2 9 CDS1 4.37 101 821		1.2
			CH.07_hs_g15868383		1.2
85	326112	EOS26043	c17_hs_g15867192[ref] gn 1 + 2151 2725 ex 1 1 CDS1 54.87 575 1272		

	333995	EOS333926	CH22_1272FG_310_19_LINK.EMAC005500.GENSCAN.107-18	1.2
	323683	CH22_3614	A380045 Hs.225023 ESTs	1.2
5	330143	EOS30074	c21_p2 g[4210430]gen3 + 184737 184848 ex 4 3 CDS1 1.71 112 111	1.2
	323789	EOS29720	c14_p2 g[6469354]lenb) gn 2 - 118577 119036 ex 1 3 CDS1 1.19 60 1517	1.2
10	324387	EOS24328	A4307836 Hs.118758 ESTs; Weakly similar to RLF [H.sapiens]	1.2
	308729	EOS08660	A1799706 Hs.208627 EST	1.2
	323939	EOS23870	AW499632 Hs.115696 ESTs	1.2
	333444	EOS33375	CH22_894FG_153_1_LINK.EMAC005500.GENSCAN.34-1	1.2
15	306302	EOS06233	A4937901 EST singleton (not in UniGene) with exon hit	1.2
	313693	EOS13624	AW469180 Hs.170651 ESTs	1.2
	316652	EOS16583	AW789249 EST cluster (not in UniGene)	1.2
	332325	EOS30256	T79488 Hs.191284 ESTs	1.2
	338235	EOS36166	CH22_3833FG_740_2_LINK.DA59H18.GENSCAN.44-2	1.2
20	319436	EOS19367	R02750 EST cluster (not in UniGene)	1.2
	312335	EOS12206	AW043620 Hs.236693 ESTs	1.2
	322109	EOS22040	AW84327 Hs.244737 ESTs	1.2
	328466	EOS2897	c_7_hs g[5869434]ref gn 1 - 15843 15900 ex 1 2 CDS1 2.36 258 1908	1.2
25	323244	EOS23175	T70731 CH.07_hs g[5888434	1.2
	312510	EOS12441	AA779807 Hs.117568 EST cluster (not in UniGene)	1.2
	314853	EOS14784	AA72932 Hs.153279 ESTs	1.2
	336946	EOS36877	CH22_4731FG_355_2_ CH22_FGENES.355-2	1.2
	303874	EOS08905	AA258921 EST cluster (not in UniGene) with exon hit	1.2
	312658	EOS12589	AA730280 Hs.120938 ESTs	1.2
	308354	EOS06265	A1611044 EST singleton (not in UniGene) with exon hit	1.2
	310073	EOS10004	C318004 Hs.148558 ESTs	1.2
	324777	EOS24708	AA744046 Hs.133350 ESTs	1.2
	300897	EOS08828	AB903556 Hs.127604 ESTs	1.2
35	303571	EOS06302	AS206065 Hs.2425 10 EST	1.2
	306358	EOS06289	AA981821 EST singleton (not in UniGene) with exon hit	1.2
	312295	EOS12226	AA578233 Hs.173863 ESTs	1.2
	319792	EOS19723	R20317 Hs.22368 ESTs	1.2
40	338546	EOS38477	CH22_7267FG_310_19_LINK.EMAC005500.GENSCAN.410-1	1.2
	314546	EOS14477	AW007211 Hs.186572 ESTs	1.2
	338484	EOS38425	CH22_7184FG_310_19_LINK.EMAC005500.GENSCAN.385-5	1.2
45	331131	EOS31062	R45797 CH22_EMAC005500.GENSCAN.385-5	1.2
	309939	EOS09870	AW419122 EST; Weakly similar to reverse transcriptase homolog [H.sapiens]	1.2
	323932	EOS32863	CH22_153FG_38_6_LINK.C20H12.GENSCAN.28-6	1.2
50	309553	EOS06584	AW196800 Hs.180842 CH22_FGENES.38_6	1.2
	318647	EOS18578	AS28152 ribosomal protein L10	1.2
	304044	EOS03975	T52479 EST cluster (not in UniGene)	1.2
	330307	EOS30238	c_7_p2 g[4877982]gbA gn 2 + 107384 107559 ex 2 4 CDS1 9.96 176 4	1.2
55	314499	EOS14430	AL044570 Hs.147975 CH107_p2 g[4877982	1.2
	338053	EOS37884	CH22_652FG_310_19_LINK.EMAC005500.GENSCAN.158-1	1.2
	332991	EOS32922	CH22_215FG_58_4_LINK.EMAC005500.GENSCAN.17-4	1.2
60	306308	EOS06239	AA948570 CH22_FGENES.58_4	1.2
	338120	EOS38051	EST singleton (not in UniGene) with exon hit	1.2
	313703	EOS13634	A161293 Hs.146882 CH22_EMAC005500.GENSCAN.195-1	1.2
	330593	EOS30494	U05053 ESTs; Weakly similar to KIAA2625 protein [H.sapiens]	1.2
	332888	EOS32817	CH22_106FG_33_7_LINK.C20H12.GENSCAN.22-9	1.2
65	302844	EOS30375	U94362 CH22_FGENES.33_7	1.2
	321755	EOS21686	A1215881 glycogenin 2	1.2
	333532	EOS33463	CH22_789FG_175_19_LINK.EMAC005500.GENSCAN.53-25	1.2
70	332863	EOS32784	CH22_81FG_28_3_LINK.C20H12.GENSCAN.16-3	1.2
	333254	EOS33185	CH22_495FG_118_2_LINK.EMAC005500.GENSCAN.2-2	1.2
75	317459	EOS17360	A1967254 CH22_FGENES.118_2	1.2
	315293	EOS15284	AW452809 ESTs	1.2
	300732	EOS00603	A1969956 Hs.257891 ESTs	1.2
	303502	EOS03433	AA488528 EST cluster (not in UniGene) with exon hit	1.2
	333126	EOS33057	CH22_355FG_82_3_LINK.EMAC005500.GENSCAN.66-10	1.2
80	332929	EOS32880	CH22_150FG_38_3_LINK.C20H12.GENSCAN.29-3	1.2
	329502	EOS29433	c10_p2 g[3883517]gbU gn 1 + 75 398 ex 1 1 CDS1 46.82 264 100	1.2
	333408	EOS33339	CH22_657FG_145_8_LINK.EMAC005500.GENSCAN.26-6	1.2
85	315472	EOS15403	AA828850 CH22_FGENES.145_8	1.2
	332690	EOS28221	c_7_hs g[5888363]ref gn 2 - 127368 127496 ex 1 5 CDS1 5.24 131 289	1.2

			CH.07_hs gl 5988363	1.2
328662	EOS28593	c_7_hs gl 6004473 ref gn 22 + 1164773 1184955 ex 7 8 CDSi 12.72 83 3916		
5	318908	EOS19738	TS5890	1.2
	303929	EOS03860	AW470753	1.2
	315712	EOS15643	A950133 Hs.120882	1.2
	307391	EOS07322	A225058	1.2
	335499	EOS35430	CH22_2851FG_571_8_LINK	1.2
10	303792	EOS03723	C75094 Hs.199839	1.2
	327287	EOS27218	c_1_hs gl 5867479 ref gn 1 - 82338 63024 ex 4 5 CDSi 11.66 187 1628	1.2
	317713	EOS17644	A733306 Hs.128071	1.2
	330137	EOS30068	c21_p2 gl 4210430 emb gn 1 - 21220 21377 ex 2 3 CDSi 1.89 158 104	1.2
15	308157	EOS08088	A510824 Hs.75968	1.2
	314462	EOS14383	ALD42699 Hs.209222	1.2
	308268	EOS08199	A0567509 Hs.172928	1.2
	321467	EOS21398	X13075	1.2
20	320993	EOS20924	AL050145 Hs.225986	1.2
	330678	EOS36709	CH22_4367FG_159_4	1.2
	319827	EOS19158	T82778	1.2
	308249	EOS08180	A560998	1.2
25	310094	EOS10025	AW450967 Hs.235240	1.2
	338902	EOS38833	CH22_4695FG_331_2	1.2
	339044	EOS36975	CH22_7944FG_LINK_DASH118.GENSCAN.27-5	1.2
	336675	EOS36606	CH22_4153FG_43_3	1.2
30	303563	EOS03494	A363799 Hs.118787	1.2
	330673	EOS36064	D57823 Hs.92862	1.2
	311814	EOS11745	AW577113 Hs.119840	1.2
	335481	EOS35412	CH22_2833FG_570_10_LINK_EM:AC005500.GENSCAN.460-4	1.2
35	314775	EOS14705	A1148680 Hs.188809	1.2
	324961	EOS24892	AA513792	1.2
	313458	EOS13389	AA007259 Hs.255853	1.2
	307074	EOS07005	A150989	1.2
	337964	EOS37895	CH22_6410FG_LINK_EM:AC005500.GENSCAN.100-9	1.2
40	328519	EOS26450	c19_hs gl 5867439 ref gn 4 + 186004 186243 ex 4 5 CDSi 4.49 240 2534	1.2
	337366	EOS37297	CH22_5551FG_736_1	1.2
	323240	EOS22271	AF089075	1.2
	307854	EOS07862	AA14692	1.2
45	328615	EOS28548	c_7_hs gl 5868239 ref gn 2 + 35214 35347 ex 3 4 CDSi 11.49 134 3651	1.2
	317787	EOS17718	AW339612 Hs.249584	1.2
	335289	EOS35219	CH22_2830FG_527_1_LINK_EM:AC005500.GENSCAN.421-1	1.2
50	323175	EOS23106	A1827137 Hs.184023	1.2
	330893	EOS30824	AA149620 Hs.71999	1.2
	306810	EOS06741	A057294	1.2
	338239	EOS38170	CH22_6833FG_LINK_EM:AC005500.GENSCAN.264-5	1.2
55	332347	EOS32278	W80326 Hs.221716	1.2
	309782	EOS09713	AW275156 Hs.156110	1.2
	322518	EOS22449	AA13446	1.2
	301187	EOS01118	AA806542	1.2
60	312129	EOS12060	AW300867	1.2
	334714	EOS34645	CH22_2024FG_421_25_LINK_EM:AC005500.GENSCAN.282-25	1.2
	316586	EOS16517	A1205077 Hs.144689	1.2
	320488	EOS20419	R31386	1.2
	327458	EOS27389	c_2_hs gl 6004455 ref gn 3 + 173257 173378 ex 5 7 CDSi 4.03 122 1184	1.2
65	336707	EOS36638	CH22_4212FG_64_3	1.2
	313561	EOS13492	AA040155	1.2
	330906	EOS30637	AA168498 Hs.72804	1.2
	330987	EOS30918	H4081 Hs.131965	1.2
	325041	EOS24072	A810182 Hs.130907	1.2
70	312225	EOS13156	A0052384 Hs.151529	1.2
	305295	EOS05228	AA687131	1.2
	306896	EOS09827	A093363	1.2
	325981	EOS25912	c21_hs gl 6588016 ref gn 3 + 105001 106038 ex 1 1 CDSi 12.69 948 567	1.2
75	332225	EOS32156	N33213 Hs.100425	1.2
	318802	EOS18733	R19443 Hs.82414	1.2
	316413	EOS18344	AA135692 Hs.144038	1.2
	312292	EOS12223	AW451893 Hs.151124	1.2
	332753	EOS23684	AA327102	1.2
80	313582	EOS13513	AW207684 Hs.13963	1.2
	317836	EOS17767	AA983913 Hs.128929	1.2
	335369	EOS32799	CH22_89FG_28_8_LINK_C20H12.GENSCAN.18-8	1.2
85	339924	EOS36855	CH22_4699FG_347_9	1.2
	327791	EOS27722	c_5_hs gl 5867977 ref gn 1 + 22491 22810 ex 6 7 CDSi 11.29 120 658	1.2

	330717	EOS30648	AA233026	Hs.23635	CH.06_hs.gi5867977	1.2
	322944	EOS22875	AA112573		EST cluster (not in UniGene)	1.2
5	312108	EOS12039	T82331	Hs.127453	ESTs	1.2
	332570	EOS32501	AA401376	Hs.28176	ESTs	1.2
	333889	EOS33811	AA132620	Hs.53542	KMA0896 protein	1.2
	310341	EOS10272	AW302773		EST cluster (not in UniGene)	1.2
	334012	EOS33943	CH22_1290FG_313_3_LINK	EM:AC005500.GENSCAN.189-3		1.2
10	318230	EOS18161	AA558125		EST cluster (not in UniGene)	1.2
	336071	EOS36002	CH22_3457FG_085_3_LINK	DJ32110.GENSCAN.21-6		1.2
	338510	EOS38441	CH22_7208FG_LINK	EM:AC005500.GENSCAN.391-22		1.2
15	334487	EOS34418	CH22_1786FG_395_9_LINK	EM:AC005500.GENSCAN.258-10		1.2
	320661	EOS20692	AA864846		EST cluster (not in UniGene)	1.2
	335200	EOS35131	CH22_2538FG_508_9_LINK	EM:AC005500.GENSCAN.401-9		1.2
20	333582	EOS33513	CH22_842FG_201_2_LINK	EM:AC005500.GENSCAN.72-3		1.2
	320789	EOS20720	R78712		EST cluster (not in UniGene)	1.2
	321185	EOS21116	H51659	Hs.189554	ESTs	1.2
	337740	EOS37671	CH22_6085FG_LINK	EM:AC000097.GENSCAN.100-6		1.2
25	315064	EOS14995	AA775208	Hs.136423	ESTs	1.2
	334883	EOS34814	CH22_2197FG_451_6_LINK	EM:AC005500.GENSCAN.340-6		1.2
	331825	EOS31736	AA411144	Hs.104788	ESTs	1.2
	319141	EOS19072	P12377		EST cluster (not in UniGene)	1.2
	333682	EOS33613	CH22_944FG_247_10_LINK	EM:AC005500.GENSCAN.102-10		1.1
30	336140	EOS36071	CH22_3530FG_705_2_LINK	DA59H18.GENSCAN.10-2		1.1
35	320727	EOS20658	U95044		EST cluster (not in UniGene)	1.1
	323947	EOS23878	AA649842	Hs.186667	ESTs	1.1
	324746	EOS24677	AA600387	Hs.222294	ESTs	1.1
	326744	EOS36675	AK031882		EST singleton (not in UniGene) with exon hit	1.1
40	326517	EOS26448	c19_hs.gi5867439[ref]	gn 1 + 44732 48355 ex 6 6 CDS1 148.22 1625 2512		1.1
	333597	EOS33528	CH22_858FG_211_5_LINK	EM:AC005500.GENSCAN.79-5		1.1
	330135	EOS30066	c21_p2.gi4456470[emb]	gn 2 - 121583 121895 ex 2 2 CDS1 18.67 303 102		1.1
45	311118	EOS15049	AA564821	Hs.143899	ESTs	1.1
	302893	EOS22824	AL117539	Hs.173515	Homo sapiens mRNA; cDNA DKFZp568H021 (from clone DKFZp568H021)	1.1
	337169	EOS37100	CH22_5189FG_563_1_LINK	CH22_FGENES.563-1		1.1
	336121	EOS36052	CH22_3510FG_701_6_LINK	DA59H18.GENSCAN.8-6		1.1
50	323332	EOS23263	AI829520	Hs.227513	ESTs	1.1
	320911	EOS20042	AI056872	Hs.133386	ESTs	1.1
	327990	EOS27921	c_6_hs.gi5868218[ref]	gn 2 - 36225 36503 ex 1 2 CDS1 16.35 279 1419		1.1
55	320425	EOS20356	C14089	Hs.201627	ESTs; Moderately similar to !!! ALU SUBFAMILY S0 WARNING ENTRY !!! [H.sapiens]	1.1
	327075	EOS27006	c21_hs.gi5631955[ref]	gn 58 + 4041318 4041431 ex 4 4 CDS1 1.79 114 1285		1.1
	314384	EOS14315	AA535840	Hs.182203	ESTs; Weakly similar to alternatively spliced product using exon 13A [H.sapiens]	1.1
	338718	EOS38947	CH22_7502FG_LINK	EM:AC005500.GENSCAN.486-9		1.1
60	330885	EOS30817	AA135606	Hs.189384	ESTs; Weakly similar to !!! ALU SUBFAMILY J WARNING ENTRY !!! [H.sapiens]	1.1
	327331	EOS27262	c_1_hs.gi5867516[ref]	gn 4 - 58506 55737 ex 2 6 CDS1 7.01 132 2349		1.1
	326714	EOS26545	c20_hs.gi5867595[ref]	gn 2 + 124440 124589 ex 5 6 CDS1 0.11 79 1020		1.1
65	316734	EOS16955	AW080237	Hs.252884	ESTs	1.1
	311660	EOS11591	AI978593	Hs.232161	ESTs	1.1
	312757	EOS12608	AI288970	Hs.133811	ESTs	1.1
	331595	EOS31617	W98502	Hs.182258	ESTs	1.1
70	337840	EOS37771	CH22_6223FG_LINK	EM:AC005500.GENSCAN.26-9		1.1
	332093	EOS32024	AA608784	Hs.112592	ESTs	1.1
	318595	EOS19526	H81361	Hs.194495	ESTs	1.1
	315990	EOS15921	AI800041	Hs.190555	ESTs	1.1
75	322438	EOS22369	W44531	Hs.167851	ESTs	1.1
	332965	EOS32896	CH22_189FG_50_3_LINK	EM:AC000097.GENSCAN.3-5		1.1
	337182	EOS37113	CH22_5204FG_570_2_LINK	FGENES.570-2		1.1
	334948	EOS34879	CH22_2269FG_465_15_LINK	EM:AC005500.GENSCAN.359-13		1.1
80	325854	EOS25795	c16_hs.gi5867069[ref]	gn 2 - 110534 110944 ex 3 3 CDS1 9.76 71 457		1.1
	337760	EOS37691	CH22_6110FG_LINK	EM:AC000097.GENSCAN.116-8		1.1
	315422	EOS15363	AW135357	Hs.192374	ESTs	1.1
85	336889	EOS38820	CH22_7746FG_LINK	DJ32110.GENSCAN.7-1		1.1
				CH22_DJ32110.GENSCAN.7-1		1.1

5	332961	EOS32862	CH22_185FG_48_18_LINK_EM:AC000097.GENSCAN.2-14	1.1
	314703	EOS14634	A1791249	1.1
	317791	EOS17722	A1801500	1.1
	333680	EOS33611	CH22_942FG_247_7_LINK_EM:AC005500.GENSCAN.102-7	1.1
10	323419	EOS22350	A248987	1.1
	338124	EOS38055	CH22_6661FG_LINK_EM:AC005500.GENSCAN.196-2	1.1
	308884	EOS08815	A1833131	1.1
	333349	EOS33280	CH22_595FG_140_3_LINK_EM:AC005500.GENSCAN.20-3	1.1
15	313150	EOS13081	A1824410	1.1
	339208	EOS39139	CH22_8146FG_LINK_FF113D11.GENSCAN.6-3	1.1
	335653	EOS35584	CH22_3013FG_590_4_LINK_EM:AC005500.GENSCAN.484-4	1.1
	319524	EOS19455	A1682865	1.1
20	301576	EOS01507	A1682905	1.1
	317588	EOS17529	A1682905	1.1
	333473	EOS33404	CH22_724FG_162_3_LINK_EM:AC005500.GENSCAN.42-10	1.1
	333949	EOS33860	CH22_1225FG_303_5_LINK_EM:AC005500.GENSCAN.162-9	1.1
25	339256	EOS39187	CH22_8207FG_LINK_BA35412.GENSCAN.7-11	1.1
	332884	EOS32815	CH22_104FG_33_5_LINK_C20H12.GENSCAN.22-7	1.1
	314660	EOS14591	AA438007	1.1
	333220	EOS33151	CH22_457FG_104_12_LINK_EM:AC000097.GENSCAN.108-11	1.1
30	308106	EOS08037	A1476803	1.1
	320709	EOS20640	AA456660	1.1
	307612	EOS07543	A2920787	1.1
	333286	EOS30217	c5_p2_g1(6671913)g1 gn 2 - 31050 31171 ex 2 7 CDS1 8.84 122 791	1.1
35	304495	EOS04426	AA446448	1.1
	310583	EOS10514	AW205632	1.1
	332965	EOS32827	CH22_117FG_35_10_LINK_C20H12.GENSCAN.24-9	1.1
	337602	EOS37533	CH22_5895FG_LINK_C20H12.GENSCAN.15-1	1.1
40	307626	EOS07557	A1300035	1.1
	334996	EOS34627	CH22_2008FG_421_5_LINK_EM:AC005500.GENSCAN.252-5	1.1
	318552	EOS18583	T33259	1.1
	337844	EOS37775	CH22_6229FG_LINK_EM:AC005500.GENSCAN.30-9	1.1
45	334823	EOS34754	CH22_2137FG_437_5_LINK_EM:AC005500.GENSCAN.301-7	1.1
	333928	EOS33859	CH22_1201FG_299_2_LINK_EM:AC005500.GENSCAN.158-5	1.1
	337503	EOS37434	CH22_5738FG_803_1_LINK_EM:AC005500.GENSCAN.299-2	1.1
	323044	EOS22975	AA148725	1.1
50	329184	EOS29095	c_x_hs_g1(586869)ref1 gn 1 + 62305 62517 ex 2 2 CDS1 17.51 213 1868	1.1
	335468	EOS35399	CH22_2819FG_567_4_LINK_EM:AC005500.GENSCAN.454-12	1.1
	338962	EOS38893	CH22_7838FG_LINK_DJ3210.GENSCAN.23-39	1.1
	323570	EOS23501	A1038823	1.1
55	333568	EOS33499	CH22_826FG_185_1_LINK_EM:AC005500.GENSCAN.84-1	1.1
	331865	EOS31796	AA425756	1.1
	336246	EOS36177	CH22_3644FG_746_5_LINK_DAS5H18.GENSCAN.48-4	1.1
	337238	EOS37169	CH22_1343FG_641_3_LINK_EM:AC005500.GENSCAN.746-5	1.1
60	305089	EOS05020	AA842822	1.1
	300997	EOS00028	A1916973	1.1
	313134	EOS13065	N83406	1.1
	337452	EOS37363	CH22_5665FG_775_1_LINK_EM:AC005500.GENSCAN.775-1	1.1
65	325453	EOS25384	c12_hs_g1(586869)ref1 gn 4 - 480706 480828 ex 3 4 CDS1 1.99 121 818	1.1
	335999	EOS35930	CH22_3380FG_657_1_LINK_DJ2467.GENSCAN.11-1	1.1
	333550	EOS33511	CH22_840FG_199_2_LINK_EM:AC005500.GENSCAN.71-2	1.1
	336836	EOS36767	CH22_4512FG_247_11_LINK_EM:AC005500.GENSCAN.279-31	1.1
70	334677	EOS34608	CH22_1986FG_418_30_LINK_EM:AC005500.GENSCAN.118-30	1.1
	329052	EOS29993	c_x_hs_g1(586869)ref1 gn 3 - 58677 58684 ex 4 11 CDS1 -8.19 118 627	1.1
	333671	EOS33602	CH22_933FG_245_5_LINK_EM:AC005500.GENSCAN.100-12	1.1
	304941	EOS04872	AA812612	1.1
75	315772	EOS15703	AW515373	1.1
				1.1

301281	EOS01212	AA843986	Hs.190586	ESTs	1.1	
303520	EOS33451	CH22_777FG_174_3_LINK_EM.AC009500.GENSCAN.53-6			1.1	
		CH22_FGENES.174_3			1.1	
5	151203	EOS15134	AI559820	Hs.199438	ESTs	1.1
	151927	EOS15858	AW025517	Hs.133250	ESTs	1.1
	317161	EOS17092	AA972165	Hs.150308	ESTs	1.1
	337692	EOS37623	CH22_6026FG_LINK_EM.AC000097.GENSCAN.78-12		1.1	
10	331472	EOS31403	N24830	CH22_EM.AC000097.GENSCAN.78-12	1.1	
			yc7a02.s1 Soares melanocyte 2NBM Homo sapiens cDNA clone IMAGE:267050 3' similar to gh[M87912]HUMALN562 Human carcinoma cell-derived Alu RNA transcript, (rRNA);contains Alu repetitive element; mRNA sequence.		1.1	
	336439	EOS36370	CH22_3859FG_827_4_LINK_EM.AC000500.GENSCAN.1-3		1.1	
15	326882	EOS26813	c20_hs gj[668250][ref] gn 2 - 167988 168179 ex 4 4 CDS1 18.99 192 2238		1.1	
			CH.20_hs gj[6682509		1.1	
	336977	EOS36908	CH22_4793FG_380_9_	CH22_FGENES.380-9	1.1	
	333953	EOS33914	CH22_1260FG_310_7_LINK_EM.AC005500.GENSCAN.167-5		1.1	
			CH22_FGENES.310_7		1.1	
20	328878	EOS28809	c_7_hs gj[6552423][ref] gn 1 + 105580 105774 ex 6 7 CDS1 2.91 195 6195		1.1	
			CH.07_hs gj[6552423		1.1	
	320415	EOS30346	D63777	Hs.75137	KIA0419 gene product	1.1
	321824	EOS24755	AI826999	Hs.224624	ESTs	1.1
	325815	EOS25746	c14_hs gj[6682483][ref] gn 1 - 129273 130754 ex 1 1 CDS0 11.82 1482 2225		1.1	
			CH.14_hs gj[6682483		1.1	
25	300483	EOS00394	N52510	Hs.186470	ESTs	1.1
	335708	EOS35639	CH22_3089FG_599_8_LINK_EM.AC005500.GENSCAN.490-11		1.1	
			CH22_FGENES.599_8		1.1	
	324575	EOS24506	AW050257	EST cluster (not in UniGene)	1.1	
	337561	EOS37882	CH22_6391FG_LINK_EM.AC005500.GENSCAN.94-1		1.1	
30			CH22_EM.AC005500.GENSCAN.94-1		1.1	
	335935	EOS35866	CH22_3313FG_646_6_LINK_EM.D124687.GENSCAN.1-5		1.1	
			CH22_FGENES.646_6		1.1	
	334914	EOS34845	CH22_2233FG_457_3_LINK_EM.AC005500.GENSCAN.348-2		1.1	
35			CH22_FGENES.457_3		1.1	
	309527	EOS09458	AW150648	Hs.75621	protease inhibitor 1 (anti-elastase); alpha-1-antitrypsin	1.1
	318901	EOS18832	AA068520	Hs.24639	ESTs	1.1
	320484	EOS20415	AA094436	Hs.155712	folistatin-like 1	1.1
	333965	EOS33986	CH22_926FG_244_1_LINK_EM.AC005500.GENSCAN.99-1		1.1	
40			CH22_FGENES.244_1		1.1	
	335860	EOS35791	CH22_3235FG_629_5_LINK_EM.AC005500.GENSCAN.519-4		1.1	
			CH22_FGENES.629_5		1.1	
	313339	EOS13270	AI682536	Hs.163495	ESTs	1.1
	300149	EOS00000	AW444918	Hs.149018	ESTs	1.1
	318112	EOS18043	AI028162	Hs.132037	ESTs	1.1
45	337907	EOS37738	CH22_8178FG_LINK_EM.AC005500.GENSCAN.9-4		1.1	
			CH22_EM.AC005500.GENSCAN.9-4		1.1	
	336917	EOS36848	CH22_4688FG_346_4_	CH22_FGENES.346-4	1.1	
	337489	EOS37420	CH22_5722FG_799_2_	CH22_FGENES.799-2	1.1	
	320112	EOS32043	T92107	Hs.163489	ESTs	1.1
50	332975	EOS32906	CH22_199FG_51_10_LINK_EM.AC000097.GENSCAN.4-12		1.1	
			CH22_FGENES.51_10		1.1	
	327805	EOS27736	c_5_hs gj[5867968][ref] gn 2 + 19562 20019 ex 1 2 CDS1 9.47 68 988		1.1	
			CH.05_hs gj[5867968		1.1	
55	339215	EOS39146	CH22_8153FG_LINK_FF113D11.GENSCAN.6-10		1.1	
			CH22_FF113D11.GENSCAN.6-10		1.1	
	311965	EOS11896	T69279	EST cluster (not in UniGene)	1.1	
	314043	EOS13974	AA427082	EST cluster (not in UniGene)	1.1	
	333447	EOS33378	CH22_154FG_154_5_LINK_EM.AC005500.GENSCAN.35-6		1.1	
60			CH22_FGENES.154_5		1.1	
	333242	EOS33173	CH22_481FG_111_6_LINK_EM.AC000097.GENSCAN.120-5		1.1	
			CH22_FGENES.111_6		1.1	
	338596	EOS38527	CH22_7343FG_LINK_EM.AC005500.GENSCAN.437-2		1.1	
			CH22_EM.AC005500.GENSCAN.437-2		1.1	
65	329989	EOS29802	c16_p2 gj[4567166][gh]A gn 2 + 72861 73052 ex 1 3 CDS1 18.02 192 590		1.1	
			CH.16_p2 gj[4567166		1.1	
	115675	EOS15806	AA652272	Hs.197320	ESTs	1.1
	330722	EOS39653	CH22_4245FG_84_2_	CH22_FGENES.84-2	1.1	
	334220	EOS34151	CH22_1503FG_359_4_LINK_EM.AC005500.GENSCAN.217-7		1.1	
70			CH22_FGENES.359_4		1.1	
	336703	EOS36934	CH22_4201FG_56_3_	CH22_FGENES.56-3	1.1	
	336397	EOS36328	CH22_3812FG_823_12_LINK_BA232E17.GENSCAN.6-11		1.1	
			CH22_FGENES.823_12		1.1	
	316105	EOS16036	AW295687	Hs.254420	ESTs	1.1
75	334661	EOS34592	CH22_1969FG_418_9_LINK_EM.AC005500.GENSCAN.279-13		1.1	
			CH22_FGENES.418_9		1.1	
	307783	EOS07714	AI347274	EST singleton (not in UniGene) with exon ht	1.1	
	333997	EOS33928	CH22_1276FG_310_22_LINK_EM.AC005500.GENSCAN.167-21		1.1	
			CH22_FGENES.310_22		1.1	
	331903	EOS18304	AA436873	Hs.29417	Homo sapiens mRNA: cDNA DKFZ568B0323 (from clone DKFZ568B0323)	1.1
80	328249	EOS28180	c_8_hs gj[6381891][ref] gn 2 - 96352 96527 ex 2 3 CDS1 6.19 176 4550		1.1	
			CH.08_hs gj[6381891		1.1	
	338251	EOS38182	CH22_6849FG_LINK_EM.AC005500.GENSCAN.270-1		1.1	
			CH22_EM.AC005500.GENSCAN.270-1		1.1	
85	323561	EOS23492	AA825426	Hs.238832	ESTs; Weakly similar to III ALU SUBFAMILY J WARNING ENTRY III [H.sapiens]	1.1
	301464	EOS01395	AA991518	Hs.253324	ESTs	1.1
	335916	EOS35847	CH22_3293FG_636_12_LINK_EM.AC005500.GENSCAN.526-12		1.1	

	321828	EO521759	X56197	CH22_FGENES.636_12	EST cluster (not in UniGene)	1.1
	327413	EO527344	c_2_hs [g]5867750[ref] gn 3 + 101410 101908 ex 4 5 CDSi 4.34 99 587	CH10_hs [g]5867750	CH22_FGENES.636-12	1.1
5	334474	EO534405	CH22_1773FG_394_5_LINK_EM-AC005500.GENSCAN.257-5	CH22_FGENES.394_5	CH22_FGENES.117-3	1.1
	336739	EO536670	CH22_4291FG_117_3	ESTs	EST singleton (not in UniGene) with exon hit	1.1
	316517	EO516448	A1784315	ESTs	EST singleton (not in UniGene) with exon hit	1.1
	325519	EO525450	c12_hs [g]6017039[ref] gn 5 - 186804 186915 ex 1 3 CDSi 8.36 112 2508	CH12_hs [g]6017039	CH22_FGENES.296_13	1.1
10	333875	EO533806	CH22_1145FG_291_11_LINK_EM-AC005500.GENSCAN.149-6	CH22_FGENES.291_11	CH22_FGENES.296-13	1.1
	338221	EO538152	CH22_6797FG_LINK_EM-AC005500.GENSCAN.246-10	CH22_EM-AC005500.GENSCAN.246-10	CH22_FGENES.316-5	1.1
15	336878	EO536809	CH22_4617FG_316_5	CH22_FGENES.316-5	CH22_FGENES.316-5	1.1
	337919	EO537850	CH22_6338FG_LINK_EM-AC005500.GENSCAN.89-5	CH22_FGENES.316-5	CH22_FGENES.316-5	1.1
	309828	EO509759	AW293999	CH22_FGENES.316-5	CH22_FGENES.316-5	1.1
	305259	EO505190	A4679225	EST singleton (not in UniGene) with exon hit	EST singleton (not in UniGene) with exon hit	1.1
20	333922	EO533853	CH22_1195FG_296_13_LINK_EM-AC005500.GENSCAN.155-16	CH22_FGENES.296_13	CH22_FGENES.296_13	1.1
	322092	EO522023	AF085833	EST cluster (not in UniGene)	EST cluster (not in UniGene)	1.1
	313356	EO513287	A1268254	ESTs	ESTs	1.1
	318847	EO518778	Z42908	ESTs	ESTs	1.1
25	337175	EO537108	CH22_5195FG_587_1	CH22_FGENES.587-1	CH22_FGENES.587-1	1.1
	339979	EO539910	CH22_4892FG_385_4	CH22_FGENES.385-4	CH22_FGENES.385-4	1.1
	312169	EO512100	A064824	ESTs	ESTs	1.1
	336198	EO536129	CH22_3595FG_719_2_LINK_DA56H18.GENSCAN.21-2	CH22_FGENES.719_2	CH22_FGENES.719_2	1.1
30	321948	EO521879	AA308612	CH22_FGENES.719_2	CH22_FGENES.719_2	1.1
	334692	EO524623	AA557552	ubiquitin-conjugating enzyme E2D 3 (homologous to yeast UBC4/5)	ubiquitin-conjugating enzyme E2D 3 (homologous to yeast UBC4/5)	1.1
	330395	EO530326	D10923	EST cluster (not in UniGene)	EST cluster (not in UniGene)	1.1
	333119	EO533050	CH22_347FG_80_4_LINK_EM-AC000097.GENSCAN.65-4	CH22_FGENES.80_4	CH22_FGENES.80_4	1.1
35	316812	EO515943	AA784950	CH22_FGENES.80_4	CH22_FGENES.80_4	1.1
	300142	EO500073	A1734319	ESTs	ESTs	1.1
	317215	EO517146	AW014242	ESTs	ESTs	1.1
	329526	EO529457	c10_p2 [g]3983506[pu]U gn 2 + 12251 12325 ex 3 3 CDSi 7.37 75 178	CH10_p2 [g]3983506	CH10_p2 [g]3983506	1.1
40	317409	EO517340	AA784958	KIAA0892 protein	KIAA0892 protein	1.1
	339230	EO539161	CH22_8171FG_LINK_BA354112.GENSCAN.1-6	CH22_BA354112.GENSCAN.1-6	CH22_BA354112.GENSCAN.1-6	1.1
45	311598	EO511529	AW023595	ESTs	ESTs	1.1
	339154	EO539095	CH22_3091FG_LINK_DA56H18.GENSCAN.69-4	CH22_DA56H18.GENSCAN.69-4	CH22_DA56H18.GENSCAN.69-4	1.1
	326725	EO526656	c20_hs [g]6552456[ref] gn 2 - 223005 223125 ex 5 6 CDSi 6.10 121 1038	CH10_hs [g]6552456	CH10_hs [g]6552456	1.1
	330952	EO530883	H02855	ESTs	ESTs	1.1
50	334621	EO534562	CH22_1928FG_412_4_LINK_EM-AC005500.GENSCAN.275-4	CH22_FGENES.412_4	CH22_FGENES.412_4	1.1
	301685	EO501616	W67730	EST cluster (not in UniGene) with exon hit	EST cluster (not in UniGene) with exon hit	1.1
	308781	EO508712	AB111707	EST singleton (not in UniGene) with exon hit	EST singleton (not in UniGene) with exon hit	1.1
55	323413	EO523344	AA248828	ESTs	ESTs	1.1
	306723	EO506654	A026151	EST singleton (not in UniGene) with exon hit	EST singleton (not in UniGene) with exon hit	1.1
	331258	EO531189	Z41777	ESTs	ESTs	1.1
	331028	EO512959	A135433	ESTs	ESTs	1.1
	333002	EO532933	CH22_228FG_59_3_LINK_EM-AC000097.GENSCAN.21-3	CH22_FGENES.59_3	CH22_FGENES.59_3	1.1
60	303011	EO502942	AF090405	EST cluster (not in UniGene) with exon hit	EST cluster (not in UniGene) with exon hit	1.1
	317897	EO517818	HA972990	ESTs	ESTs	1.1
	326779	EO526710	c_7_hs [g]5868309[ref] gn 4 + 41570 41839 ex 1 5 CDSi 2.65 70 5365	CH10_hs [g]5868309	CH10_hs [g]5868309	1.1
	338707	EO538638	CH22_7487FG_LINK_EM-AC005500.GENSCAN.482-2	CH22_EM-AC005500.GENSCAN.482-2	CH22_EM-AC005500.GENSCAN.482-2	1.1
65	337974	EO537905	CH22_6427FG_LINK_EM-AC005500.GENSCAN.106-3	CH22_EM-AC005500.GENSCAN.106-3	CH22_EM-AC005500.GENSCAN.106-3	1.1
	332854	EO532785	CH22_71FG_22_1_LINK_C20H12.GENSCAN.15-2	CH22_FGENES.22_1	CH22_FGENES.22_1	1.1
70	311225	EO511156	AW451982	ESTs	ESTs	1.1
	337054	EO537025	CH22_5018FG_465_19	CH22_FGENES.465-19	CH22_FGENES.465-19	1.1
	319357	EO519288	F13425	ESTs	ESTs	1.1
	332958	EO532889	CH22_183FG_48_15_LINK_EM-AC000097.GENSCAN.2-11	CH22_FGENES.48_15	CH22_FGENES.48_15	1.1
75	309834	EO509565	AW193825	EST singleton (not in UniGene) with exon hit	EST singleton (not in UniGene) with exon hit	1.1
	321171	EO521102	A1784410	ESTs	ESTs	1.1
	316440	EO516371	A1954796	ESTs	ESTs	1.1
	311655	EO511596	AW294254	ESTs	ESTs	1.1
	327548	EO527479	c_3_hs [g]5867797[ref] gn 1 + 36165 35332 ex 3 7 CDSi 6.42 64 12	CH10_hs [g]5867797	CH10_hs [g]5867797	1.1
80	314940	EO514871	AW452768	ESTs	ESTs	1.1
	326401	EO526332	c19_hs [g]5867355[ref] gn 1 + 36165 35332 ex 9 11 CDSi 0.41 168 788	CH19_hs [g]5867355	CH19_hs [g]5867355	1.1
	338947	EO538978	CH22_3759FG_815_3_LINK_BA32817.GENSCAN.1-24	CH22_FGENES.815_3	CH22_FGENES.815_3	1.1
85	322297	EO522228	W78548	ESTs; Moderately similar to IIII ALU SUBFAMILY SC WARNING ENTRY IIII [H.sapiens]	EST singleton (not in UniGene) with exon hit	1.1
	309977	EO509908	AW451603	EST singleton (not in UniGene) with exon hit	EST singleton (not in UniGene) with exon hit	1.1

	333466	EOS33397	CH22_717FG_161_2_LINK.EM.ACO05500.GENSCAN.42-2		
			CH22_FGENES.161_2		1.1
	329170	EOS29101	c_x_hs gl[588693]ref gn 2 - 67624 68019 ex 6 8 CDSI 3.30 96 1882		1.1
5	329479	EOS29410	c10_p2 gl[598352]gb A gn 3 - 7425 7561 ex 1 3 CDSI 4.33 137 22		1.1
			CH_10_p2 gl[598352]		1.1
	329668	EOS26999	c20_hs gl[655245]ref gn 1 - 146725 146836 ex 11 11 CDSI 1.84 113 767		1.1
			CH_20_hs gl[655245]		1.1
10	319064	EOS11295	H06538 Hs.12270	ESTs	1.1
	302988	EOS02919	W23986 Hs.34578	alpha2-3-sialyltransferase	1.1
	327687	EOS27618	c_4_hs gl[5667847]ref gn 1 - 166299 169362 ex 2 3 CDSI -0.28 70 782		1.1
			CH_14_hs gl[5667847]		1.1
	339413	EOS39344	CH22_8405FG_LINK.DU579N16.GENSCAN.5-8		1.1
15	306156	EOS06087	AA918274 Hs.76067	heat shock 27KD protein 1	1.1
	302988	EOS02919	D59968	EST cluster (not in UniGene)	1.1
	325447	EOS25378	c12_hs gl[5869941]ref gn 3 - 975490 973261 ex 2 3 CDSI 9.16 142 1026		1.1
			CH_12_hs gl[5869941]		1.1
20	322696	EOS22627	A1064724 Hs.228468	ESTs	1.1
	329959	EOS29890	c18_p2 gl[5103803]gb A gn 3 + 188050 188193 ex 8 8 CDSI 2.01 144 361		1.1
			CH_18_p2 gl[5103803]		1.1
	312628	EOS12559	AA632817 Hs.190316	ESTs	1.1
	339305	EOS39236	CH22_8282FG_LINK.BA35412.GENSCAN.21-3		1.1
25	311829	EOS11760	A078483 Hs.134548	ESTs	1.1
	303270	EOS03291	AI_130519 Hs.106362	ESTs	1.1
	321226	EOS21157	AA311443 Hs.251416	Homo sapiens mRNA; cDNA DKFZp586E2317 (from clone DKFZp586E2317)	1.1
	335827	EOS35758	CH22_3200FG_820_1_LINK.EM.ACO05500.GENSCAN.512-1		1.1
30	336677	EOS36608	CH22_4155FG_43_5_LINK.EM.ACO05500.GENSCAN.512-1		1.1
	330091	EOS30012	c19_p2 gl[6015314]gb A gn 1 - 5768 5835 ex 4 9 CDSI 2.88 68 162		1.1
			CH_19_p2 gl[6015314]		1.1
35	339313	EOS39244	CH22_8272FG_LINK.BA35412.GENSCAN.22-11		1.1
	319936	EOS19867	W22152	EST cluster (not in UniGene)	1.1
	332858	EOS32789	CH22_76FG_24_1_LINK.C20H12.GENSCAN.16-6		1.1
			CH22_FGENES.24_1		1.1
40	319530	EOS15561	AA648355 Hs.185155	ESTs; Weakly similar to echinoderm microtubule-associated protein-like EMAP2 [H.sapiens]	1.1
	332995	EOS32926	CH22_219FG_58_2_LINK.EM.ACO05500.GENSCAN.19-2		1.1
			CH22_FGENES.58_2		1.1
	333441	EOS33372	CH22_691FG_151_5_LINK.EM.ACO05500.GENSCAN.32-5		1.1
			CH22_FGENES.151_5		1.1
45	333496	EOS33427	CH22_748FG_168_6_LINK.EM.ACO05500.GENSCAN.47-5		1.1
			CH22_FGENES.168_6		1.1
	339188	EOS39119	CH22_8123FG_LINK.DA59H18.GENSCAN.72-16		1.1
			CH22_DA59H18.GENSCAN.72-16		1.1
	336981	EOS36912	CH22_4818FG_397_7_LINK.AW229539 Hs.212069	ESTs	1.1
	312142	EOS12073	AW229539 Hs.212069	ESTs	1.1
	315779	EOS15710	AW015736 Hs.211378	ESTs	1.1
50	318596	EOS18527	AI470235 Hs.172698	EST	1.1
	335701	EOS35632	CH22_3062FG_599_1_LINK.EM.ACO05500.GENSCAN.490-2		1.1
			CH22_FGENES.599_1		1.1
	319395	EOS19326	AW062570 Hs.13809	ESTs	1.1
55	304236	EOS04167	W93278	EST singleton (not in UniGene) with exon hit	1.1
	307264	EOS07195	A1022211	EST singleton (not in UniGene) with exon hit	1.1
	334066	EOS33997	CH22_1344FG_327_21_LINK.EM.ACO05500.GENSCAN.181-23		1.1
			CH22_FGENES.327_21		1.1
	327042	EOS26973	c21_hs gl[6531965]ref gn 18 - 1380806 1381443 ex 1 5 CDSI 30.85 638 943		1.1
			CH_21_hs gl[6531965]		1.1
60	326025	EOS26996	c17_hs gl[5867176]ref gn 1 + 70864 70915 ex 6 8 CDSI -1.48 62 127		1.1
			CH_17_hs gl[5867176]		1.1
	325609	EOS25540	c14_hs gl[5866996]ref gn 28 - 981751 981849 ex 1 10 CDSI 1.46 99 101		1.1
			CH_14_hs gl[5866996]		1.1
65	319983	EOS19914	T81429	EST cluster (not in UniGene)	1.1
	334298	EOS34229	CH22_1589FG_372_4_LINK.EM.ACO05500.GENSCAN.232-5		1.1
			CH22_FGENES.372_4		1.1
	323203	EOS23134	AA203135 Hs.130186	ESTs	1.1
	305700	EOS05631	AA815428	EST singleton (not in UniGene) with exon hit	1.1
70	313504	EOS10335	AI334078 Hs.126438	ESTs	1.1
	310716	EOS10647	AI689818 Hs.192413	ESTs	1.1
	327048	EOS26980	c21_hs gl[6531965]ref gn 24 - 1924026 1924110 ex 2 6 CDSI 9.43 85 1012		1.1
			CH_21_hs gl[6531965]		1.1
	313749	EOS13680	AW460376 Hs.130803	ESTs	1.1
	307041	EOS06972	AI144243	EST singleton (not in UniGene) with exon hit	1.1
75	323294	EOS22325	AF077208	EST cluster (not in UniGene)	1.1
	326416	EOS26347	c19_hs gl[5867382]ref gn 3 - 45283 45375 ex 3 3 CDSI 5.65 93 923		1.1
			CH_19_hs gl[5867382]		1.1
	333947	EOS33878	CH22_1221FG_303_1_LINK.EM.ACO05500.GENSCAN.162-5		1.1
			CH22_FGENES.303_1		1.1
80	324609	EOS24540	AW299534	EST cluster (not in UniGene)	1.1
	330057	EOS29688	c17_p2 gl[6478962]gb A gn 3 + 75145 75287 ex 3 3 CDSI -2.56 143 150		1.1
			CH_17_p2 gl[6478962]		1.1
	337893	EOS37534	CH22_589FG_LINK.C20H12.GENSCAN.15-2		1.1
			CH22_C20H12.GENSCAN.15-2		1.1
85	332913	EOS32644	CH22_134FG_36_18_LINK.C20H12.GENSCAN.28-17		1.1
			CH22_FGENES.36_18		1.1

5	310026	EOS09957	T24895	Hs.100891	ESTs	1.1
	330153	EOS30084	c21_p2 gi 4325335 gb A	gn 2 + 148951 147475 ex 2 2 CDS 25.45 525 233	CH.1_p2 gi 4325335	1.1
10	334118	EOS34049	CH22_1396FG_330_19_LINK	EMAC005050.GENSCAN.185-20	CH22_FGENES.330_19	1.1
	324795	EOS24726	A484481	Hs.141579	ESTs	1.1
15	323530	EOS32461	M51682	Hs.1735	inhb; beta B (activin AB beta polypeptide)	1.1
	332045	EOS31979	A446019	Hs.201561	ESTs	1.1
20	334532	EOS34463	CH22_1834FG_402_13_LINK	EMAC005050.GENSCAN.269-13	CH22_FGENES.402_13	1.1
	329762	EOS29693	c14_p2 gi 6048280 emb	gn 3 + 127744 127878 ex 2 4 CDS 11.66 135 1054	CH.14_p2 gi 6048280	1.1
25	332909	EOS32840	CH22_130FG_36_13_LINK	C20H12.GENSCAN.26-10	CH22_FGENES.36_13	1.1
	321253	EOS21184	A1699484	EST cluster (not in UniGene)	CH22_FGENES.343_12	1.1
30	330672	EOS36503	CH22_4007FG_843_12_LINK	D367H16.GENSCAN.15-13	CH22_FGENES.843_12	1.1
	328768	EOS28899	c_7_hs gi 6017031 ref	gn 5 - 223741 224238 ex 1 1 CDS 30.00 498 5285	CH.07_hs gi 6017031	1.1
35	334335	EOS34266	CH22_1627FG_375_12_LINK	EMAC005050.GENSCAN.235-12	CH22_FGENES.375_12	1.1
	334063	EOS33994	CH22_1341FG_327_17_LINK	EMAC005050.GENSCAN.181-20	CH22_FGENES.327_17	1.1
40	333011	EOS32942	CH22_235FG_61_3_LINK	EMAC000097.GENSCAN.23-3	CH22_FGENES.61_3	1.1
	304677	EOS04608	AA548071	EST cluster (not in UniGene) with exon hit	CH22_FGENES.375_12	1.1
45	313948	EOS13879	AW452823	Hs.135258	ESTs	1.1
	334358	EOS34289	CH22_1652FG_378_1_LINK	EMAC005050.GENSCAN.238-1	CH22_FGENES.378_1	1.1
50	326479	EOS28410	c_7_hs gi 5888449 ref	gn 1 - 331 569 ex 1 31 CDS 18.51 230 2100	CH.07_hs gi 5888449	1.1
	335813	EOS35744	CH22_3185FG_618_1_LINK	EMAC005050.GENSCAN.510-1	CH22_FGENES.618_1	1.1
55	312430	EOS12361	AW139117	Hs.117494	ESTs	1.1
	324783	EOS24714	AA640770	EST cluster (not in UniGene)	CH22_FGENES.119-18	1.1
60	337776	EOS37707	CH22_6132FG_LINK	EMAC000097.GENSCAN.119-18	CH22_FGENES.119-18	1.1
	327205	EOS27136	c_1_hs gi 5867447 ref	gn 5 + 167335 167576 ex 9 9 CDS 15.50 242 256	CH.01_hs gi 5867447	1.1
65	315198	EOS15129	AT741 506	Hs.186753	ESTs; Weakly similar to IIII ALU SUBFAMILY J WARNING ENTRY IIII [H.sapiens]	1.1
	336135	EOS36066	CH22_3525FG_704_3_LINK	DA5H18.GENSCAN.9-5	CH22_FGENES.704_3	1.1
70	318558	EOS18489	AW402677	Hs.90372	ESTs	1.1
	329152	EOS28083	c_6_hs gi 5865000 ref	gn 1 - 73981 74203 ex 1 18 CDS 31.69 223 3411	CH.06_hs gi 5865000	1.1
75	330211	EOS30142	c_5_p2 gi 6013562 gb A	gn 1 + 59158 59215 ex 2 2 CDS 4.20 68 184	CH.05_p2 gi 6013562	1.1
	339280	EOS39211	CH22_823FG_LINK	BA39412.GENSCAN.14-12	CH22_FGENES.14-12	1.1
80	332045	EOS31976	AA481253	Hs.155045	bromodomain adjacent to zinc finger domain; 2A	1.1
	313597	EOS13528	AW162283	Hs.249090	ESTs	1.1
85	329503	EOS29434	c10_p2 gi 3983517 g u	gn 2 - 1801 1837 ex 1 4 CDS 4.33 137 101	CH.10_p2 gi 3983517	1.1
	333488	EOS33419	CH22_740FG_167_3_LINK	EMAC005050.GENSCAN.45-10	CH22_FGENES.167_3	1.1
90	311960	EOS11891	AW440133	Hs.189990	ESTs	1.1
	320590	EOS20321	U67058	Hs.168102	Human proteinase activated receptor-2 mRNA; 5'UTR	1.1
95	334047	EOS33978	CH22_1325FG_326_5_LINK	EMAC005050.GENSCAN.175-6	CH22_FGENES.326_5	1.1
	304782	EOS04713	AA582081	EST singleton (not in UniGene) with exon hit	CH22_FGENES.326_5	1.1
100	324231	EOS24162	W08027	EST cluster (not in UniGene)	CH22_FGENES.326_5	1.1
	327212	EOS27143	c_1_hs gi 5867463 ref	gn 1 - 42306 42424 ex 5 13 CDS 6.58 117 325	CH.01_hs gi 5867463	1.1
105	335857	EOS35788	CH22_3232FG_629_1_LINK	EMAC005050.GENSCAN.519-1	CH22_FGENES.629_1	1.1
	317775	EOS17706	AA974603	Hs.181123	ESTs	1.1
110	331053	EOS30984	N70242	Hs.183146	ESTs	1.1
	339040	EOS35871	CH22_3318FG_646_13_LINK	DJ24807.GENSCAN.1-12	CH22_FGENES.646_13	1.1
115	322568	EOS22489	W87342	Hs.208652	ESTs	1.1
	314091	EOS14022	AI253112	Hs.133540	ESTs	1.1
120	313570	EOS13501	AA041455	Hs.209312	ESTs	1.1
	300667	EOS00898	AA565209	Hs.190216	ESTs	1.1
125	314544	EOS14475	AA398018	Hs.250835	ESTs	1.1
	326321	EOS28232	c_7_hs gi 58686373 ref	gn 7 - 1029614 1029673 ex 1 3 CDS -2.40 80 448	CH.07_hs gi 58686373	1.1
130	310979	EOS10910	AW445166	Hs.170802	ESTs	1.1
	310730	EOS10861	AI539421	Hs.160300	ESTs	1.1
135	319471	EOS18402	AW137225	Hs.146874	ESTs	1.1
	315533	EOS15464	AW206191	Hs.152774	ESTs	1.1
140	325751	EOS25682	c14_hs gi 6682474 ref	gn 4 + 130437 130520 ex 6 7 CDS 0.22 84 1666	CH.14_hs gi 6682474	1.1
	318780	EOS18711	R90906	Hs.113307	ESTs	1.1
145	313271	EOS13202	AW444819	Hs.144851	ESTs; Weakly similar to C09F5.2 [C.elegans]	1.1
	304546	EOS04477	AA480074	EST singleton (not in UniGene) with exon hit	CH22_FGENES.326_5	1.1
150	330618	EOS30549	X55590	Hs.73839	noncatalytic; RNase A family; 3 (eosinophil cationic protein)	1.1

	33931	EOS32862	CH22_152FG_38_5_LINK_C20H12.GENSCAN.29-5		
			CH22_FGENES.38_5	1.1	
	336602	EOS36533	CH22_4047FG_372_4_LINK_EMA.C005500.GENSCAN.232-4	1.1	
			CH22_FGENES.372_4	1.1	
5	311185	EOS11116	A1038294	ESTs	1.1
	337585	EOS37516	CH22_5873FG_LINK_C20H12.GENSCAN.5-3	1.1	
			CH22_C20H12.GENSCAN.5-3	1.1	
	310249	EOS10180	AW071751	ESTs	1.1
	314578	EOS14509	AA410183	ESTs	1.1
10	310750	EOS10681	A1573163	ESTs	1.1
	333668	EOS33999	CH22_1245FG_307_4_LINK_EMA.C005500.GENSCAN.165-5	1.1	
			CH22_FGENES.307_4	1.1	
	316133	EOS16094	A187742	ESTs	1.1
	308337	EOS06268	A1608947	EST singleton (not in UniGene) with exon hit	1.1
15	328160	EOS26091	c17_hs_gi[5867254]ref gn 6 - 112000 112137 ex 2 4 CDS; 8.01 138 1952	1.1	
			CH17_hs_gi[5867254]	1.1	
	336623	EOS36594	CH22_3406FG_669_12_LINK_DJ3210.GENSCAN.9-17	1.1	
			CH22_FGENES.669_12	1.1	
	323479	EOS23410	AA278246	EST cluster (not in UniGene)	1.1
20	330900	EOS36021	CH22_3477FG_699_2_LINK_DJ3210.GENSCAN.23-20	1.1	
			CH22_FGENES.699_2	1.1	
	311192	EOS11123	AW237220	ESTs	1.1
	335081	EOS35012	CH22_2409FG_498_4_LINK_EMA.C005500.GENSCAN.384-6	1.1	
			CH22_FGENES.498_4	1.1	
25	309519	EOS09450	AW148940	EST	1.1
	321172	EOS21103	H49180	ESTs	1.1
	301576	EOS01907	T57905	EST cluster (not in UniGene) with exon hit	1.1
	323012	EOS22943	A1832201	ESTs	1.1
	319328	EOS19459	R06873	ESTs	1.1
30	329336	EOS27699	c14_p2_gi[6672062]ref gn 2 + 33990 34098 ex 3 4 CDS; 9.11 109 2222	1.1	
			CH14_p2_gi[6672062]	1.1	
	320223	EOS02554	AB019571	EST cluster (not in UniGene) with exon hit	1.1
	334433	EOS34364	CH22_1731FG_385_8_LINK_EMA.C005500.GENSCAN.249-6	1.1	
			CH22_FGENES.385_8	1.1	
35	304747	EOS04678	AA577816	EST singleton (not in UniGene) with exon hit	1.1
	333270	EOS33201	CH22_513FG_121_1_LINK_EMA.C005500.GENSCAN.4-11	1.1	
			CH22_FGENES.121_1	1.1	
	307054	EOS06885	A148181	EST	1.1
	320764	EOS23695	R73070	ESTs	1.1
40	321523	EOS21454	H78472	ESTs; Weakly similar to cDNA EST Yk414c8.3 comes from this gene [C.elegans]	1.1
	322114	EOS22045	AA643791	ESTs	1.1
	303592	EOS03513	AA377444	EST cluster (not in UniGene) with exon hit	1.1
	322924	EOS22655	AA686253	ESTs	1.1
	311179	EOS11110	AB80843	ESTs	1.1
45	318601	EOS18532	T39921	EST cluster (not in UniGene)	1.1
	309791	EOS09722	AW276176	ribosomal protein; large; P0	1.1
	333882	EOS33813	CH22_1150FG_292_4_LINK_EMA.C005500.GENSCAN.150-4	1.1	
			CH22_FGENES.292_4	1.1	
	337645	EOS37576	CH22_5960FG_LINK_EMA.C000097.GENSCAN.10-8	1.1	
			CH22_EMA.C000097.GENSCAN.10-8	1.1	
50	335623	EOS36564	CH22_2983FG_584_2_LINK_EMA.C005500.GENSCAN.478-2	1.1	
			CH22_FGENES.584_2	1.1	
	314745	EOS14676	AA564489	ESTs	1.1
	330790	EOS30721	T48536	ESTs	1.1
55	332071	EOS32002	AA588594	ESTs	1.1
	312005	EOS11936	T78450	ESTs	1.1
	330994	EOS03625	AA019806	apocerebellar ataxia 7 (olivopontocerebellar atrophy with retinal degeneration)	1.1
	330739	EOS30670	AA293477	ESTs	1.1
	303042	EOS02973	AF129532	EST cluster (not in UniGene) with exon hit	1.1
60	323091	EOS23022	AW014094	ESTs	1.1
	328620	EOS28751	c_7_hs_gi[5868330]ref gn 1 + 90448 90602 ex 3 4 CDS; 10.20 157 5634	1.1	
			CH07_hs_gi[5868330]	1.1	
	300472	EOS00403	T06022	hydroxymethylbilane synthase	1.1
	310645	EOS10576	AI420742	ESTs	1.1
65	323238	EOS32169	NS3400	ESTs	1.1
	300986	EOS00897	AA564740	ESTs	1.1
	330437	EOS30368	H32730-HT2827	Fibrinogen, A Alpha Polypeptide, A1; Splice 2, E	1.1
	302292	EOS02223	AF067797	EST cluster (not in UniGene) with exon hit	1.1
70	330138	EOS30069	c21_p2_gi[4210430]ref gn 1 - 22334 22460 ex 3 3 CDS; 16.96 127 105	1.1	
			CH21_p2_gi[4210430]	1.1	
	323952	EOS32883	CH22_178FG_48_8_LINK_EMA.C000097.GENSCAN.2-4	1.1	
			CH22_FGENES.48_8	1.1	
	319601	EOS19832	T77139	RNA helicase-related protein	1.1
	321166	EOS21097	AA411263	ESTs	1.1
75	336227	EOS36158	CH22_3625FG_730_2_LINK_DA5H18.GENSCAN.36-2	1.1	
			CH22_FGENES.730_2	1.1	
	302332	EOS02263	A1833168	Homo sapiens Chromosome 16 BAC clone QT9875K-A-32B3	1.1
	313800	EOS13731	AW261132	ESTs	1.1
80	338356	EOS36287	CH22_8326FG_LINK_BA35412.GENSCAN.31-1	1.1	
			CH22_BA35412.GENSCAN.31-1	1.1	
	324512	EOS24443	AW050125	EST cluster (not in UniGene)	1.1
	318235	EOS19166	F11330	ESTs	1.1
	303032	EOS02093	Y13303	disintegrin protease	1.1
85	338316	EOS38247	CH22_6944FG_LINK_EMA.C005500.GENSCAN.304-2	1.1	
			CH22_EMA.C005500.GENSCAN.304-2	1.1	
	333964	EOS33995	CH22_1241FG_305_2_LINK_EMA.C005500.GENSCAN.164-2	1.1	

				CH22_FGENES.306_2	1.1		
	312758	EOS12689	AA721107	Hs.202604	ESTs	1.1	
	338178	EOS38109	CH22_6728FG_LINK_EM:AC005500	GENSCAN.219-6		1.1	
5	315199	EOS15130	AA877996	Hs.125376	ESTs	1.1	
	312321	EOS12252	R66210	Hs.186937	ESTs	1.1	
	338765	EOS38698	CH22_7588FG_LINK_EM:AC005500	GENSCAN.518-1		1.1	
	330547	EOS30478	U32989	Hs.183671	tryptophan 2,3-dioxygenase	1.1	
10	315368	EOS15299	AW291563	Hs.152495	ESTs	1.1	
	328691	EOS28622	c_7_hs	gl 5588001 ref	gn 7 - 579598 57964 ex 2 3 CDSi 12.78 67 4326	1.1	
					CH107_hs	gl 5588001	1.1
	329179	EOS29110	c_x_hs	gl 5588704 ref	gn 2 + 181639 181815 ex 3 4 CDSi 0.32 177 1539	1.1	
15	327072	EOS27003	c21_hs	gl 5531963 ref	gn 55 - 3796429 3797197 ex 4 4 CDSi 9.33 769 1270	1.1	
					CH121_hs	gl 5531965	1.1
	312056	EOS11987	T83748	Hs.189712	ESTs	1.1	
	339128	EOS39059	CH22_8046FG_LINK_EM:AC005500	GENSCAN.55-2		1.1	
20					CH22_DA59H18	GENSCAN.55-2	1.1
	307646	EOS07577	A0302236		EST singleton (not in UniGene) with exon hit	1.1	
	318198	EOS19129	F07354		EST cluster (not in UniGene)	1.1	
	338556	EOS38487	CH22_7283FG_LINK_EM:AC005500	GENSCAN.417-8		1.1	
					CH22_EM:AC005500	GENSCAN.417-8	1.1
25	306143	EOS06074	AA918314		EST singleton (not in UniGene) with exon hit	1.1	
	332364	EOS32315	M11433	Hs.101850	retinol-binding protein 1; cellular	1.1	
	325100	EOS25031	T10265	Hs.116122	ESTs; Weakly similar to coded for by C. elegans cDNA yk303.5 [C.elegans]	1.1	
	308939	EOS09770	AW296076		EST singleton (not in UniGene) with exon hit	1.1	
	312180	EOS12111	A1248285	Hs.118348	ESTs	1.1	
	330385	EOS33016	AA448740	Hs.31386	ESTs; Highly similar to secreted apoptosis related protein 1 [H.sapiens]	1.1	
	315882	EOS15813	A031297	Hs.123310	ESTs	1.1	
30	325843	EOS25774	c16_hs	gl 5552453 ref	gn 1 - 7128 7232 ex 1 3 CDSi 1.87 107 182	1.1	
					CH116_hs	gl 5552453	1.1
35	330783	EOS30714	D06060	Hs.34812	ESTs	1.1	
	317224	EOS17155	D56760	Hs.8122	ESTs	1.1	
	319342	EOS15875	AW297979	Hs.170988	ESTs	1.1	
	333524	EOS33455	CH22_781FG_175_10_LINK_EM:AC005500	GENSCAN.53-15		1.1	
					CH22_FGENES.175_10		1.1
	302357	EOS02288	X03178	Hs.198246	group-specific component (vitamin D binding protein)	1.1	
	308630	EOS09761	AW294725		EST singleton (not in UniGene) with exon hit	1.1	
40	321489	EOS21420	AW392474	Hs.172759	ESTs; Moderately similar to [H.sapiens]	1.1	
	312304	EOS12235	AA491949	Hs.183359	ESTs	1.1	
	322026	EOS21957	AA233527	Hs.213289	low density lipoprotein receptor (familial hypercholesterolemia)	1.1	

Table 2 provides the nucleic acid and protein sequence of the CBF9 gene as well as the Unigene and Exempral accession numbers for CBF9.

5

TABLE 2 CBF9 DNA and Protein Sequences

CBF9 DNA sequence

Gene name: ESTs
Unigene number: Hs.157601
Probeset Accession #: W07459
Nucleic Acid Accession #: AC005383
Coding Sequence: 328-2751 (underlined sequences correspond to start and stop codons)

15	1	11	21	31	41	51	
	GACAGTGTTC	GCGGCTGCAC	CGCTCGGAGG	CTGGGTGACC	CGCGTAGAAG	TGAAGTACTT	60
	TTTATTATTC	AGACCTGGGC	CGATGCCGCT	TAAAAAAGC	CGAGGGGGCTC	TATGCACCTC	120
	CCTGGCGGTA	GTTCCTCCGA	CCTCAGCCGG	GTCCGGTCTGT	GCCGCCCTCT	CCCGAGAGAG	180
	ACAAACAGGT	GTCCCACTGT	GCAGCCCGGC	CCCGGGCGCC	CCTCCTGTGA	TCCCGTAGCG	240
	CCCCCTGGCC	CGAGCCCGGC	CGGGGTCTGT	GAGTAGAGCC	GCCCGGGCAC	CGAGCGCTGG	300
	TGCGCGTCT	CCTTCGGTTA	TATCAACATG	CCCCCTTCC	TGTTGCTGGA	GGCGCTCTGT	360
	GTTTCTCTGT	TTTCCAGAGT	GCCCCCATCT	CTCCCTCTCC	AGGAAGTCCA	TGTAAGCAA	420
	GAACCACTCG	GGAAAGTTTC	AGCTGCCAGC	AAAAATGATG	GGTGTCTGGC	TGCAGTGGAC	480
	ATCATGTTTC	TGTTAGATGG	GTCTAACAGC	CTCGGGAAG	GGAGCTTTGA	AAGGTCGAAG	540
	CACCTTGCCA	TCACAGTCTG	TGACGGTCTG	GACATCAGCC	CCGAGAGGGT	CAGATGGGGA	600
	GCATTCCAGT	TCAGTTCCAC	TCCTCATCTG	GAATTCCTCT	TGGATTCAIT	TTCAACCCAA	660
	CAGGAAGTGA	AGGCAAGAAT	CAAGAGGATG	GTTTTCAAA	GAGGGCGCAC	GGAGACGGAA	720
	CTTGCTCTGA	AATACCTTCT	GCACAGAGGG	TTGCGTGGAG	GCAGAAATGC	TTCTGTGCC	780
	CAGATCCCTA	TCATCGTCAC	TGATGGGAAG	TCCAGGGGGG	ATGTGGCACT	GCCATCCAG	840
	CAGCTGATTG	AAAGGGGTGT	CACCTGTGTT	GCTGTGGGGG	TCAGTTTCCC	CAGGTGGGAG	900
	GAGCTGCATG	CACCTGGCCAG	CGAGCCTAGA	GGGCGAGCAG	TGCTGTGTGG	TGAGCAGGTG	960
	GAGGATGCCA	CAACGGCCCT	CTTCAGCACC	CTCAGCAGCT	CGGCATCTG	CTCCAGCGCC	1020
	ACCCGACAGT	CGAGGCTCGA	GGCTCACCCC	TGTGAGCACA	GGACGCTGGA	GATGTCCTGG	1080
	GAGTTCGCTG	GCATGCCCCC	ATGCTGGAGA	GGATCGGGGC	GGACCTTTGC	GGTGTGCTGT	1140
	GCACACTGCT	CCTTCTACAG	CTGGAAGAGA	GTGTTCTCTA	CCACCCCTGC	CACCTGTGCT	1200
	AGGAGCACCT	CGCCAGGCC	CTGTGACTCG	CAGCCCTGCC	AGAATGGAGG	CACATGTGTT	1260
	CCAGAAGGAC	TGACGCGCTA	CCAGTGCCCT	TGCCCGCTGG	CTTTTGGAGG	GGAGGCTTAT	1320
	TGTGTCCTGA	AGCTGAGCCT	GGAAATGCAG	GTGCACTCCC	TCCTTCTGCT	GGACAGCTCT	1380
	CGGGGCACCA	CTCTGGACGG	CTTCTCGCG	GCCAAAGTGT	CTGTGAAGAG	GTTTGTGCGG	1440
	GCCGTGCTGA	CGAGGAGACT	TGCGGCCCGA	GTGGGTGTGG	CACATACAG	CAGGAGGACT	1500
	CTGCTGCGGG	TGCCCTGTGG	GGAGTACCAG	GATGTGCCCT	CCACTGTCTG	GAGCCTCGAT	1560
	GGCATTCCTC	TCCGTGCTGG	CCCCACCCTG	ACGGGCGATG	CCTTGGCGCA	GGCGGCGAG	1620
	CGTGGCTTGG	GAGGCGCCAC	CAGGACAGGC	CAGGACCGGC	CACGTAGAGT	GGTGTGTTTG	1680
45	CTCACTGAGT	CACACTCCGA	GGATGAGGTT	GCGGGCCGAG	CGCGTCACGC	AAGGGCCGCA	1740
	GAGCTGTCTC	TGCTGGGTGT	AGGCAGTGAG	GCCGTGCGGG	CAGAGCTTGA	GAGAGTACCA	1800
	GGCAGCCCAA	AGCATGTGAT	GGTCTACTCG	GATCTCTCAG	ATCTGTTCAA	CCAAATCCCT	1860
	GAGCTGTGAG	GGAAGCTGTG	CAGCCGCGAG	CGCCAGGGT	GCCCGGACACA	AGCCCTGGAC	1920
	CTCGCTTCTA	TGTTGGACAC	CTCTGCCCTA	GTAGGGCCCG	AGAATTTTGC	TCAGATGACG	1980
50	AGCTTTGTGA	GGAAGCTGTG	CTTCCAGTTT	GAGGTGAACC	CTACAGCTTGC	CAGAGTCCGC	2040
	CTGCTGCTGT	ATGGCAGCCA	GGTGACAGCT	GCTTTCGGGC	TGGACACCAA	ACCCACCCGG	2100
	GCTGCGATGC	TGCGGGCCAT	TAGCCAGGCC	CCCTACCTAG	TGTGGGTGGG	GCCGCTCGGC	2160
	ACCCGCTGCG	TGCACATCTA	TGACAAAGTG	ATGACCGTCC	GAGAGGGGTG	CGCGCTTGCT	2220
	CTCCCCAAAG	CTGTGTTGGT	GCTCACAGGC	GGGAGAGGCG	CAGAGGATGC	AGCCCTTCTC	2280
55	CGCCAGAAGC	TGAGGACAA	TGGCATCTCT	GTCTTGGTCG	TGGCGCTGGG	GCTGTGCTTA	2340
	AGTGAAGGTC	TGCGGAGGCT	TGCAGGTCCC	CGGGAATCCC	TGATCCACGT	GCGAGCTTAC	2400
	GCCGACCTGC	GTTACACACA	GGACGTGCTC	ATTGAGTGGC	TGTGTGGAGA	AGCCACGATC	2460
	CCAGTCAACC	GTGTCAAAAC	CAGCCCGTGC	ATGAATGAGG	GCGAGCTGCT	CTCTGCAAGT	2520
	GGGAGCTTAC	GCTGCAAGTG	TGCGGATGGC	TGGAGGGGCC	CCCACTGCGA	GAACCGTAG	2580
60	TGAGGCTCTT	GCTCTGTATG	TGTGAGCCAG	GGATGGATT	TGAGAGCGCC	CCTGAGGCAC	2640

ATGGCTCCCG TGCAGGAGGG CAGCAGCCGT ACCCCTCCCA GCAACTACAG AGAAGGCCTG 2700
 GGCATCGAAA TGGTGCCTAC CTTCGTGAAT GTCTGTGCC CAGGTCTCTA GAATGTCCTG 2760
 TTCCCCCGGT GCCCAGGACC ACTATCTCA CTGAGGGAGG AGGATGTCCC AACTGCAGCC 2820
 ATGCTGCTTA GAGACAAGAA AGCAGCTGAT GTCAACCACA AACGATGTTG TTGAAAAGTT 2880
 TTGATGTGTA AGTAAATACC CACTTCTGTG ACCTGTGTG CCTTGTGTAG GCTATGTGAT 2940
 CTGCCACCTT TCCCTTGAGG ATAAACAAGG GGTCCTGAAG ACTTAAATTT AGCGGCCTGA 3000
 CGTTCTTTTG CACACAATCA ATGCTCGCCA GAATGTGTTT GACACAGTAA TGCCCGACAG 3060
 AGGCCTTTAC TAGAGCATCC TTTGGACGGC GAAGGCCACG GCCTTTCAAG ATGGAAGACA 3120
 GCAGCTTTTC CACTTCCCA GAGACATTCT GGATGCATTT GCATTGAGTC TGAAAGGGGG 3180
 CTTGAGGGAC GTTGTGACT TCTGGCCGAC TGCCCTTTGT GTGTGGAAGA GACTTGGAAA 3240
 GGCTCTCAGC TGAATGTGAC CAATTAAACA GCTTGGTTGA TGATGGGGGA GGGGCTGAGT 3300
 TGTGCAATGG CCCAGGTCGT GAGGGCCACG TAAATCGTT CTGAGTCGTG AGCAGTGTCC 3360
 ACCTTGAAG TCTTC

CBF9 Protein sequence

Gene name: ESTs
 Unigene number: Hs.157601

Protein Accession #: none found

Signal sequence: 1-17
 Transmembrane domains: none found
 VGV domains: 49-223; 341-518; 529-706
 EGF domains: 298-333; 715-748
 Cellular Localization: plasma membrane

1 11 21 31 41 51
 MPFFLLLEAV CVFLFSRVPP SLPLEQEVHS KETIGKISAA SKMMWCSAAV DIMFLLDGSN 60
 SVGKGSFERS KHFAITVCDG LDISPERVRV GAFQFSSTPH LEFFLDLSFT QQEVKARIKR 120
 MVFKGGRTET ELALKYLLHR GLPGGRNASV PQILIIITDG KSGGDVALPS KQLKERVTV 180
 FAVGVRFPRW EELHALASEP RGQHVLLAQ VEDATNGLFS TLSSSAICSS ATPDCRVYEAH 240
 PCEHRTLMEV REFAGNAPCW RGSRRTLAVL AAHCFFYSWK RVFLTHPATC YRTTCPGPCD 300
 SQPCQNGGTC VPEGLDGYQC LCPLAFGGEA NCALKLSLEC RVDLLFLDLS SAGTITLDGFL 360
 RAKVFVKRFV RAVLSSEDSRA RVGVATYSRE LLVAVPVGEY QDVVDLVWSL DGIPFRGGPT 420
 LTGSALRQAA ERGFGSATRT GQDRPRRVVV LLTESHSEDE VAGPARHARA RELLLLGVGS 480
 EAVRAELEEI TGSPKHMVMY SDPQDLFNQI PELQKLCER QRPGCRTQAL DLVFMLDTSA 540
 SVGPENFAQM QSFVRSCALQ FEVNDVDTQV GLVVYGSQVQ TAPGLDTKPT RAAMLRAISQ 600
 APYLGGVGGA GTALLHIYDK VMTVQRGARF GVPKAVVLT GGRGAEDAAV PAQKLRRNGI 660
 SVLVVVGVEF LSEGLRRLAG PRDSLHVAE YADLRHYQDV LIEMWCGEAK QPVNLCKPSS 720
 CMNEGSCVLQ NGSYRCKCRD GWBGFHCENR EWSSCSVCVS QGWILETPLR HMAVPVQEGSS 780
 RTPPSNVREG LGTEMVPTFW NVCAPGF